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# EDITORIAL

A LARGE part of the literature dealing with tuberculosis has been devoted to the tubercle bacillus. Its behaviour in different media and in the body, the effect on the body of a primary infection and, again, of reinfection, and more recently the action of the component parts of the bacillus, have been subjects of extensive research.

There can be no disagreement as to the importance of these matters, but in our endeavours to discover all about the bacillus let us not forget the body. Dr. Hall's article on Tuberculosis in China introduces us to a type of the disease rare in this country; yet the bacillus is the same.

Mr. Hamerton's interesting paper will stimulate thought on an aspect of tuberculosis which has been neglected. Oxen and pigs are highly susceptible, but why should their cousin the camel remain immune in spite of the opportunity it has of becoming infected in India and Egypt?

Why should certain animals, immune to tuberculosis in their natural surroundings, become susceptible in captivity? Why should others, like the zebra, keep their immunity in captivity? Why should certain races of mankind show considerable resistance to tuberculosis in their native homes, but become very susceptible on moving to other countries?

Mr. Hamerton suggests that tuberculosis is the child of civilisation, for he says: "It seems probable that there is no tuberculosis under wholly natural conditions of life."

Partial immunity may be acquired by infection, and the vast amount of research on this subject and on attempts to obtain protection by B.C.G. and other methods is most valuable, but we have long been of the opinion that the importance of natural immunity has not been appreciated.

# PROBLEMS IN APPLIED MEDICINE

## IS THE DELICATE CHILD MORE LIKELY THAN THE STRONG ONE TO GROW INTO THE ADULT CONSUMPTIVE?

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TWENTY-ONE years of tuberculosis work has been for me twenty-one years of slow and sometimes painful learning. I am still learning, and have yet much to learn. Fifteen to twenty years ago this paper would have been clearer, more precise, and no doubt more useful; fifteen to twenty years hence I shall write no longer, so I trust my present shortcomings will be forgiven.

As time passes the statistics to be considered become vaster and their study increasingly arduous, while the modern efficiency of radiography and increased experience in the interpretation of films are constantly discrediting our earlier case records, so that we are driven back upon impressions. This applies not only to my own work, but also from various experienced Tuberculosis Officers to whom application for illustrative statistics has been made came the same reply: None available; only impressions.

On *a priori* grounds it would be expected that debilitated children whose resistance was therefore presumed to be low would be the most likely to develop tuberculosis, but experience of a large number of contacts and the following up of contacts for many years belies the expectation, for the frail children grow into frail but non-tuberculous adults, whereas the young adult and adult cases of florid or more chronic tuberculous disease come, alas! from among the apparently healthy children. Of delicate children in Lancashire referred to the Tuberculosis Officer because tuberculosis was suspected, 59 per cent. were rejected as non-tuberculous, and of these only 0·91 per cent. returned later as definite cases of tuberculosis in young adult age, and this supports the impression previously gathered by the Lancashire staff. In Leeds also it has been remarked that the young adults from tuberculous families who come to the dispensary with active pulmonary tuberculosis are

not as a rule those who were delicate in early life, but who as children " never ailed anything."

Scotland has provided the most definite figures on the subject that have yet appeared, and these were printed in a paper by Drs. P. L. McKinlay and E. Watt of the Department of Health for Scotland in the *Lancet* of August 11, 1934. These observers were considering the problem more especially from the point of view of the School Medical Officer. It is recognised that some attributes, such as overweight, are of significance in predisposing to the onset of disease or in curtailing life, and it is certain, too, that such conditions as septic tonsils or other focal sepsis, if untreated, predispose to or cause more serious illness in later life; but of the significance of many, perhaps most, variations from the normal little is known, and prolonged and careful study is requisite. The aim of Drs. McKinlay and Watt was to discover whether by routine clinical examination it was possible to predict the type of child likely to become tuberculous later, and rather than commence a *de novo* research the Dundee statistics were studied, and among the selected school records information was sought as to the earlier life of patients notified as tuberculous. A control series was also compiled. The children were of the same social class, and were examined by similar Medical Officers, so avoiding differences in medical assessment. The patients chosen numbered ninety-seven and were between the ages of 15 and 25.

Concerning infectious diseases, the following percentage table quoted from the article cited shows the comparative incidence among the ultimately tuberculous and the controls:

| | *Ultimately Tuberculous.* | *Controls.* |
|---|---|---|
| Measles ... ... ... ... ... ... | 80·4 | 77·3 |
| Scarlet fever ... ... ... ... ... | 18·5 | 7·2 |
| Diphtheria ... ... ... ... ... | 4·1 | 3·0 |
| Whooping-cough ... ... ... ... | 60·8 | 58·7 |
| Chicken-pox ... ... ... ... ... | 31·9 | 24·7 |
| Bronchitis and pneumonia ... ... ... | 8·2 | 6·1 |

With the exception of scarlet fever, no difference which might be considered significant appears.

The following table shows similar percentage results elicited by a comparison of the external condition of the children:

| | *Ultimately Tuberculous.* | *Controls.* |
|---|---|---|
| Insufficient clothing ... ... ... ... | 1·9 | 0·7 |
| Dirty clothing ... ... ... ... ... | 5·3 | 1·4 |
| Clean heads ... ... ... ... ... | 73·5 | 82·9 |
| Nits ... ... ... ... ... ... | 21·1 | 12·7 |
| Clean bodies ... ... ... ... ... | 86·7 | 85·1 |
| Flea-bitten bodies ... ... ... ... | 7·9 | 11·3 |

Allowing for the small numbers studied, this does suggest that dirty clothing and dirty heads are more frequent among those who later become tuberculous.

Now a percentage table comparing the physical condition of the subjects of this investigation:

| | *Ultimately Tuberculous.* | *Controls.* |
|---|---|---|
| Enlarged tonsils ... ... ... ... | 18·5 | 26·4 |
| Enlarged submaxillary glands ... ... | 17·2 | 21·2 |
| Enlarged cervical glands ... ... ... | 3·9 | 6·3 |
| Nutrition — Above average ... ... ... | 45·7 | 47·5 |
| Nutrition — Average ... ... ... ... | 51·6 | 48·2 |
| Nutrition — Below average ... ... ... | 2·6 | 4·2 |
| Anæmia ... ... ... ... ... ... | 4·6 | 8·5 |
| Bronchial catarrh ... ... ... ... | 7·2 | 1·4 |
| Rickets ... ... ... ... ... ... | 2·6 | 0·7 |

So that in this series no real difference due to the state of nutrition is manifest.

The average weights in pounds and heights in inches provide food for thought.

| | *Weight.* | *Height.* | *Age.* |
|---|---|---|---|
| Ultimately tuberculous ... ... | 61·4 | 50·7 | 10·6 |
| Males control ... ... ... | 63·5 | 51·4 | 10·6 |
| Ultimately tuberculous ... ... | 63·5 | 51·9 | 10·6 |
| Females control ... ... ... | 60·1 | 50·5 | 10·3 |

In males the weights of the ultimately tuberculous is lower than the controls, but among the females higher, but the differences are not considered important. There is then no real difference between the height and weight of the ultimately tuberculous and that of the average school child of the same age. The children dealt with do not necessarily come from tuberculous households, but so far as this research carries us no noteworthy difference can be detected.

This Scottish work shows what use can be made of the vast array of figures compiled each year by the School Medical Officers. The authors themselves criticise it and suggest the possible inclusion of vital capacity readings, chest measurements, and intercurrent illnesses. They also rightly remark that the numbers are too small for any epoch-making conclusions, and draw attention to the negativity of the findings. But it remains the most valuable contribution today available on the subject of this paper, and coincides with my personal impressions.

Although we can all of us recall instances of healthy children who suddenly develop young adult phthisis, and these make the greater impression

on our minds, on sober reflection we can also remember delicate children who have expectedly become phthisical later on.

A boy of 10 was thin and delicate, and tuberculosis was suspected, but he continued in normal health, and at 14 went to work in a garage just at the commencement of the war. The adult garage workers were busy, and a large proportion of hard manual work fell to the lot of this willing but frail youth. At 16 he developed a subacute young adult phthisis and died within a year.

Adverse physical conditions presented to a boy of subnormal development may break down his resistance with greater facility than in the case of a normal lad.

Another boy of 10 was seen as a contact in August, 1928. He had always been delicate, but clinical and radiographic examinations were negative. Nevertheless his brother had died from tuberculosis at 21 a short time previously, so this boy was sent to a children's sanatorium, where he remained for two years and three months. After leaving school he went to work, and remains at work today, but a skiagram taken in February, 1935, showed a coarse mottling in both upper zones. Precautionary measures which might be called extreme have not prevented tuberculosis. This delicate boy has developed phthisis, despite every care and without unduly hard work.

On the whole I believe that just as *a priori* surmises require correction, so our later impressions need reconsideration, and that sooner or later we shall be driven to conclude that the debilitated child is just as likely, no more and no less, to develop young adult or adult phthisis as the robust or normal schoolboy.

It is difficult to co-ordinate physical development and resistance to disease. Susceptibility to colds, measles, diphtheria, or scarlet fever may be found in children thin, fat, or of average build and strength. The exact factors concerned we do not yet know, but such research as has been carried out in Scotland which has here been summarised leads the way to further knowledge.

The thin man lives longer than the stout—we do not exactly know why—and it hardly leads us further to suggest that some endocrine unbalance in the stout may be the basis of the difference. The study and elucidation of the many-sided problems of tuberculosis cannot be divorced from those of general medicine, and research in the tuberculosis field provides an attractive base for progress in manifold directions.

# GENERAL ARTICLES

## TUBERCULOSIS IN CHINA

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Tuberculosis has always been a disease of civilisation, and as China was civilised many centuries before the Christian era, she has paid for her civilisation more than the usual toll of tuberculous disease.

In the *Canon of Medicine*, said to have been written by the Emperor Huang-ti, who lived some time between the years 2698 and 2598 B.C., descriptions of the "lung cough" and "lung fever" are such as to be easily interpreted as pulmonary tuberculosis. In the historical records of the Han Dynasty, Queen Chao Fei-yen (32-8 B.C.) is described as being "so thin that she could dance on the palm of the hand." She was frequently ill and had a capricious appetite, eating only when the Emperor himself prepared her food. She suffered from frequent hæmoptyses and was sterile. One may safely assume that she suffered from pulmonary tuberculosis.

In the *Chin Kuei Yao Lueh*, written by the Chinese Hippocrates, Chang Chung-ching, about A.D. 198, abscess of the lung is recognised as a different disease from the better-known "atrophy" or "enfeeblement" of the lungs. In the Sui Dynasty (A.D. 589) a long account of the causes and symptoms of the "enfeebling chronic cough" and the "enfeebling chronic fever" is given in the medical book called the *Chao Shih Ping Yuan*. Little of value is added by writers of the Sung and Yuan Dynasties (A.D. 962-1280), but descriptions of the symptoms and causes of tuberculosis are clear and definite in the writings of the Ming Dynasty (A.D. 1368-1644), by which time the name still applied to the disease—viz., "lao cheng," or the "wasting disease"—has come into common usage. It was recognised by writers of this period that tuberculosis was a family disease, and it was said that, though contracted *in utero*, symptoms did not develop till between the ages of fifteen and twenty-five years. The development of disease with or at a

variable period after a hæmoptysis was well recognised. Hoarseness and uncontrollable diarrhœa were recognised as fatal signs. The *spes phthisica* is accurately described. The heroine of one of the most popular novels of the early Ch'ing Dynasty (1644), *The Dream of the Red Chamber*, died as the result of a large pulmonary hæmorrhage. The description of her disease makes it clear that tuberculosis was at that time a common disease looked upon with fear and horror by all who came in contact with it.

There seems no reasonable doubt, therefore, that tuberculosis is referred to in Chinese literature over a period of many centuries, and that the disease has been prevalent in China from the earliest times of which there are records.

An estimate of the incidence, mortality, and types of tuberculosis existing in China today cannot be made with any degree of accuracy. Such vital statistics as are available are unreliable, and refer only to the few foreign-controlled concessions and Treaty Ports in which commercial endeavour and industrialisation have created conditions differing entirely from those existing in other parts of the country. The Chinese are still essentially an agricultural people living in small towns and villages from which no information is forthcoming. Pan[1] has recently examined the literature relating to tuberculosis in China, and finds it both inadequate and unreliable for the purpose of estimating the epidemiology of the disease. Even in such cities as Shanghai and Hong Kong, with well-established public health services, the majority of the native inhabitants when ill consult only old-style physicians, and causes of death are seldom accurately determined. Statistics based on records from modern hospitals are further misleading unless the conditions peculiar to each are taken into account. For example, the Red Cross Hospital in Shanghai has a well-established tuberculosis service, and a considerable proportion of the beds in the medical department are controlled by this service; whereas the Peiping Union Medical College attempts to exclude from admission to the medical service patients who need treatment for pulmonary tuberculosis. For such reasons no statistical study of tuberculosis in China can be made, and it is necessary to discuss this problem on the basis of clinical impressions and personal experience.

It is inevitable that in a country the size of China, containing as it does areas differing considerably in density of population and in ease of communication, the incidence, distribution, and the types of disease will differ in different localities. On the other hand, the China which is known to the West, comprising the east-coast cities and the cities available for trade by means of the great water-ways of the Yangtze and the Yellow River (but with the exception of the Treaty Ports), is remarkably homogeneous.

Customs and mode of life differ but little between one city and another. Diet is similar in form, differing only in the vegetables eaten and in the main cereal used, be it rice, wheat, or oatmeal. The family is universally the unit of control, and in village or in town, in the rich house or in the poor, the family crowds in on itself, so that every house is over-populated. Habits are such as to ensure the dissemination of a bacillary infection within the family. In the home, as also in the village inns, the brick bed is common to all, sick or well. Spitting is universal and an accepted habit in homes, in public places, and in the streets. Food is taken from a common bowl with the chopsticks which convey it to the individual mouth. In the well-to-do home, servants must be considered as units of the family, since it is with them that the children live.

Cow's milk has never been an article of diet in China. Cattle native to China, such as the water buffalo, are used as draught animals only. Thus bovine infection does not occur under natural conditions. Under foreign tuition the value of cow's milk as an article of infant diet is being learned, and milch cattle are being imported, without adequate control, chiefly from Japan, and milk infected with tubercle bacilli is now being sold, at least in Shanghai, if not elsewhere also. The frequency with which tubercle bacilli are found in milk samples examined in Shanghai has increased from 8 per cent. in 1930 to 23 per cent. in 1933.[2]

**Types of Disease.**

In spite of the absence of a bovine infection, the types of disease commonly referred to as "surgical," and thought to be the result of bovine infection —namely, tuberculosis of bones, joints, superficial lymph nodes, and the mesentery—are extremely common, at least in North China.[3] In mission hospitals, patients with such conditions fill most of the beds.[4] That they are caused by the human type of bacillus is undoubted. They occur, however, in a somewhat different age-group from cases in Europe. It is the young adult, and not the child, who is the victim of such disease. Of the 50 patients referred during a two-month period to the tumour clinic of the Peiping Union Medical College Hospital for treatment for tuberculous adenitis, 9 (18 per cent.) were below the age of fifteen years, 27 (54 per cent.) were between the ages of sixteen and twenty-five, and 14 (28 per cent.) were twenty-six years of age or over. Heine[5] found that the average age of female patients operated on in Shanghai for tuberculous glands in the neck was eighteen years. The diagnosis of tuberculosis of the cervical lymph nodes was recorded in 118 in-patients of the Peiping Union Medical College between the years 1931 and 1934, and of these only 21 were below the age of twelve years. There does not seem to be any marked difference

in the course of such disease from that in Western patients, though it is frequently more extensive, but it is possible that in Chinese patients pulmonary lesions occur somewhat more frequently in conjunction with these peripheral human bacillus infections.

Pulmonary tuberculosis is widely diffused throughout the population. In a survey of the X-ray findings in 1,000 apparently healthy young adults applying for entrance as students or members of staff of the Peiping Union Medical College, Hall and Chang[6] found that 81·9 per cent. had evidence of intrathoracic tuberculous infection, and of these 6·3 per cent. had lesions which appeared to be active and potentially progressive.

The disease appears in the majority of instances in a peculiarly chronic and non-toxic form. One is frequently amazed to find it so advanced as to be completely beyond the hope of cure in patients who, to within a few months of presenting themselves for examination, have had practically no symptoms and suffered not at all from their disease.

A young woman recently seen in the tuberculosis clinic of the Peiping Union Medical College Hospital, suffering from bilateral, far-advanced cavitated pulmonary tuberculosis, tuberculosis of the larynx and tuberculosis of the intestine, had been attending classes regularly until one month before this diagnosis was made. Bumé[7] has had similar experiences in Shanghai, and states: " Some forms of the disease are so chronic that we see Chinese patients walking about, who make us think that a foreigner in similar circumstances would have been dead a long time."

Hæmoptysis is frequently an early symptom of this type of disease, and has been known and dreaded as such for many generations in China. Of 108 in-patients in the Peiping Union Medical College Hospital in whom far-advanced pulmonary tuberculosis was found, 33 had had hæmoptysis as an initial symptom, in many cases years before the development of other symptoms or signs of pulmonary tuberculosis. Eighty-nine of this group had had hæmoptysis at some time during the course of their disease.

In some cases hæmoptysis may be the only symptom of tuberculosis, which, though widespread, may heal completely without giving further evidence of its presence. The X-ray picture of the lungs of such an individual is shown in Fig. 1:

> This young man, twenty-eight years of age, felt and looked perfectly well. On physical examination there was no evidence of disease in any organ. He had worked as a telegraph linesman for several years before the picture was taken. He remembered no exposure to individuals suffering from tuberculosis. At the age of eighteen he had had a small hæmoptysis lasting over a few days for which he had had no treatment.

Of more importance and of more frequent occurrence is the clinical tuberculosis of extremely insidious onset, which remains symptomless until a large area of the lung is involved. Such a condition is exemplified by the following case:

A young woman entered the Peiping Union Medical College as a medical student at the age of twenty-two in the year 1927. Her father had died of pulmonary tuberculosis in 1916. One brother had

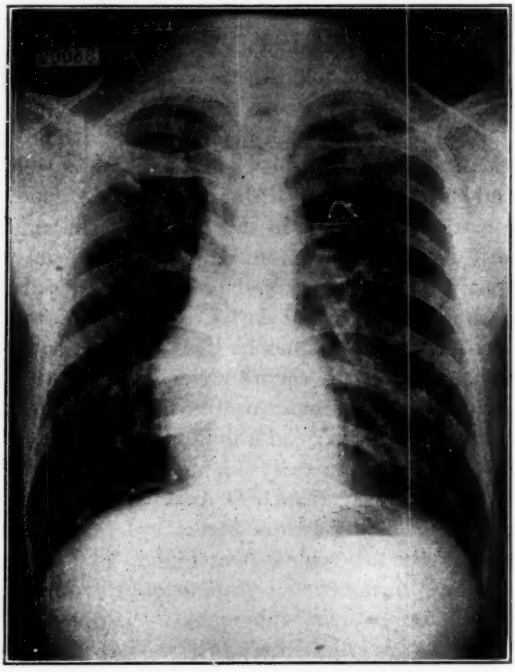

FIG. 1.

tuberculosis of the neck glands, and one other brother and one sister were healthy. Physical examination was entirely normal at that time. An X-ray film showed an irregular calcified patch in one of the lower bronchial lymph nodes of the left side, but the lung parenchyma was clear. In 1930 a second lung X-ray showed essentially the same findings. Some weight was lost during the interne year, but was regained one year later. Between 1932 and 1934 the weight steadily increased. In November, 1934, the patient developed a somewhat hard and troublesome cough, raising very occasionally a small quantity of sputum. Apart from this she felt perfectly well

and did not tire at work, in spite of carrying a heavy research programme. She had always been above the average in resistance to respiratory infections. Nineteen days after the development of the cough the X-ray shown in Fig. 2 was taken. It shows a wide involvement of the right upper lobe by a productive lesion, which, however, does not extend to the apex. In addition there are two small exudative lesions in the left lower lobe, one near the hilum and the other beneath the pleura at the lung periphery.

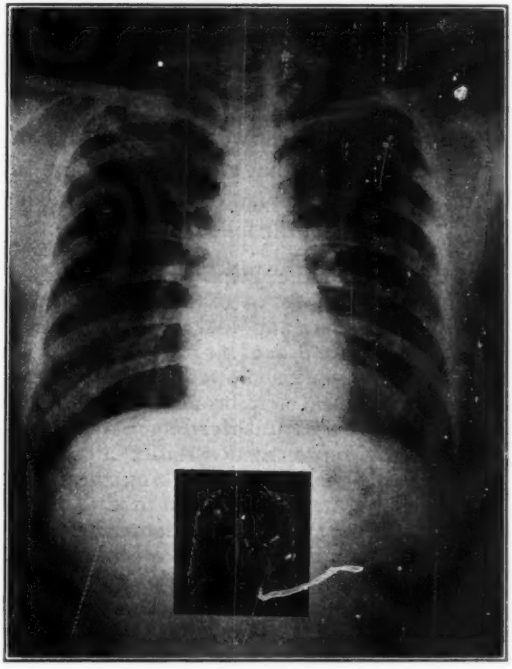

FIG. 2.

Treatment in such conditions must be radical and prolonged if relapse and insidious extension of the lesion are to be prevented. The results and effect of treatment obviously cannot be judged by temperature reactions or instability of the pulse, as such patients remain free from fever and other toxic symptoms until the disease is widespread.

It was hoped that the blood sedimentation test would be of value in determining when treatment might be discontinued and in demonstrating the liability to, or the actual occurrence of, relapse or extension of the disease. Such limited experience as we have of this test, however, shows

that it has no value in this direction, as extension may occur without any increase in the sedimentation rate. Such lesions frequently shrink rapidly under treatment by bed rest, and assume a hard and strand-like appearance, as seen in the X-ray picture; but unless time is given for them to stabilise, the lesion is seen to extend as soon as the patient is allowed out of bed.

Lesions of this nature can be kept in check, though they may not heal completely, under treatment by artificial pneumothorax. The economic situation in China is such as to force us to relax such lungs by means of small artificial pneumothoraces, allowing the patient to return to his occupation after three months. Many such patients are able to work hard so long as pneumothorax can be maintained, and in most cases it is found that the lesion is satisfactorily healed after two years of such treatment. It is sometimes found, however, that even two years of relaxation has not caused the lesion to fibrose to the extent that allows the patient, in the absence of such relaxation, to work without spread of the disease. This state of affairs is well illustrated in the record of the following patient:

> A young man entered the Peiping Union Medical College as a medical student in September, 1930. His family and past history were entirely negative. He felt and looked well. Physical examination was negative. The X-ray film of his lungs taken as part of the routine entrance physical examination showed a fibrosed tuberculous infiltration along the left vertebral stem bronchus in the first interspace area, with slight thickening of the trunks leading to the apex. It was thought at that time that this represented a stable latent lesion; and he was allowed to start work. In February of 1931 he developed a cold in the head, followed by a slight but non-productive cough. Physical examination at that time showed some depression of the breath sounds in the left upper area and a few large bronchial râles throughout both lung fields. X-ray showed extension of the lesion with diffuse mottling and increase of the thickened trunks in the first interspace area near the hilum. He admitted that he was not feeling as well as usual and tended to tire in the evenings. He was put to bed in the hospital and the cough disappeared in two weeks. During these two weeks the rectal temperature was never above 37·6° C., and seldom as high as that. The pulse-rate was never beyond 90 per minute. Treatment by artificial pneumothorax was started at this time, and though the diseased area was never satisfactorily collapsed, the patient was able to work without symptoms, and with a steady gain in weight during this period. In March, 1933, the lung was allowed to re-expand and an X-ray in June showed that the lesion in the left upper area was sharply defined and had contracted considerably. In October, however, though there had been no symptoms at all during the interval, new infiltration was shown in the X-ray in the second interspace area. The patient was therefore sent to a sanatorium, where he remained at complete bed rest till July, 1934, by which time

the lesions had again consolidated and almost completely lost their fuzzy outline, as seen in the X-ray. He returned home and was allowed only minor activities till September, when he was allowed to attend classes in the mornings only. By December he had lost slightly in weight (though still above the average weight for his height), and X-ray again showed extension of the lesions in both the first and second interspace areas.

The only possible criterion for adequacy of treatment is the serial X-ray picture taken at intervals of about three months. Even in the absence of cavitation a patient should not be allowed out of bed at all until two X-rays taken three months apart show that no change has taken place in the size or nature of the lesion. When such a stage is reached, the patient is allowed out of bed for very short periods each day during the next three months, and if the next X-ray still shows stability, activities are gradually increased until the patient is able to return to normal life. Frequent X-rays are still necessary during the next two years, and extension of the lesion necessitates the return of the patient to bed until stability is again obtained. This is the ideal at which we aim, but which we are seldom able to realise.

Surgical measures are of assistance, and probably more frequently applicable when the disease is so chronic and non-toxic. Phrenic evulsion, by allowing greater relaxation, ensures more rapid stabilising of the lesion. Chinese patients with extensive fibrotic and cavitated lesions are generally in a state of comparative well-being, or can rapidly be improved by a short period of adequate bed rest, and are then good surgical risks. Thoracoplasties are well borne, and are frequently necessary to allow large cavities to close, or to allow adequate contraction to occur in a densely fibrotic area.

Even in the presence of advanced disease which is actively progressive a state of general well-being is maintained for a considerable period. In 22 of 108 in-patients of the Peiping Union Medical College Hospital in whom a diagnosis of far-advanced pulmonary tuberculosis was made (most of whom entered the hospital for unassociated conditions) there was nothing in the history or symptoms to suggest such a diagnosis, which was made only after the condition was revealed by physical, X-ray, and sputum examinations. Death usually occurs as a result of general dissemination of the tuberculosis throughout the organs of the body, and frequently from tuberculous meningitis. Intestinal tuberculosis is a frequent complication, and gradual inanition due to lack of assimilation of food is a common mode of death. Cachexia with the well-known malar flush and bright and shining eye is not seen. It was with something of a shock that the writer, during a visit to the Papworth Tuberculosis Colony, was reminded of this form of " consumption " in walking through the wards containing advanced cases. Tuberculosis in China is a " phthisis " rather than a consumption.

Another somewhat remarkable finding in China is the rarity of amyloid or lardaceous degeneration as a complication of tuberculosis, or indeed of any chronic suppurative processes. Chronic suppurative processes are very frequently found both with and without tuberculosis, and yet this diagnosis has never been confirmed either clinically or at autopsy on Chinese patients in this hospital. Ku and Simon[8] report similar experiences, and state further that the condition is rare in Japanese. It would seem, therefore, that in China tuberculosis is a disease better tolerated than it is in the West. Acute forms are extremely rare. In most cases there is a long latent period during which symptoms are absent, though lesions are extending. Large areas of the lung may be involved without appreciably affecting the well-being of the patient. Even in the presence of advanced disease toxic symptoms are not prominent, and when present can, as a rule, rapidly be relieved by adequate rest.

One is naturally interested in speculating why tuberculosis in China is found in this chronic non-toxic form. Rich[9] states that the nature and extent of a lesion will vary in relation to the *virulence* and *number* of the organisms causing the lesion, and the state of *allergy* and the *resistance* of the host. Each of these four variables will be considered.

*Virulence.*—As long ago as 1898 Theobald Smith[10] suggested "that the saprophytic life of tubercle bacilli in sputum may be the cause of a very slow downward descent of the invasive power, which in the course of one or more generations may become perceptible both to the bacteriologist and to the clinician, and express itself to the statistician in the gradual falling curve of tuberculosis."

It has recently been shown that any strain of tubercle bacillus may be dissociated into R (resistant) and S (sensitive) colonies, which vary considerably from each other not only in biological characteristics, but also in virulence. Each strain will contain a greater or lesser number of R and S colonies, with perhaps many indefinite and intermediate forms as well.[11] Sabin (personal communication) has recently found that the S variant is much richer in the toxic carbohydrate fraction, and so in addition to possessing higher virulence will also produce a higher degree of intoxication. We are endeavouring to obtain satisfactory dissociation of tubercle bacilli recovered from Chinese patients to ascertain whether perhaps the S variant is less abundant than in Western strains.

*Numbers.*—According to Rich[9] it is the number of bacilli initiating a lesion which is largely responsible for the type of lesion produced. Typical tubercles of the productive type are formed where few bacilli aggregate, be they non-pathogenic acid-fasts or highly virulent tubercle bacilli. On the other hand, if large numbers of bacilli are thrown together at one spot, an

exudative and destructive reaction will follow, irrespective of the state of allergy of the host. A sufficient number of bacilli are essential for necrosis of any appreciable extent, but the number of bacilli necessary to effect necrosis will in general be inversely proportional to the degree to which allergic hypersensitivity is developed, though even with active allergy the number must be more than a few. Pinner[12] sums up the situation by stating "that for any given state of allergy the dosage of the reinfecting bacilli is the factor which determines whether this allergy means immunity or hypersusceptibility—prolongation of life or shortening of life." Multiplication of bacilli *in situ* is much enhanced when the inoculum is large, and is further favoured by the rapid destruction and caseation provoked by the exudative reaction. When such lesions occur in pulmonary tissue, bacilli are expectorated in enormous numbers with the sputum (Opie[13]), but when the lesions are of a more productive nature, even though cavities be formed, bacilli are found in smaller numbers, though probably over longer periods. The latter is certainly true of Chinese patients in whom, even in the presence of a cavity, daily sputum examinations fail to reveal tubercle bacilli for weeks at a time. It does not, however, give us the clue to chronicity, but simply shows that chronic forms breed chronic forms by keeping dosages of reinfection small.

*Allergy.*—It is felt by the author that the degree of tissue hypersensitivity may be related to the size and frequency of primary infections and subsequent reinfections.

It is suggested that the exquisite sensitivity of raw South African natives (48·6 per cent. react to tuberculin in a dilution of 1 : 10,000,000)[12] is caused by large primary infections without further reinfections in their villages, and that this predisposes them to rapidly destructive lesions when reinfection (liable also to be large) is met with under the unfavourable environment of the gold-mine. Shipman's[15] observations on nurses in California show that the state of skin sensitivity has some bearing on the type of lesion produced. He found that nurses who broke down with tuberculosis, and who were known to have been highly sensitive before their breakdown, developed typical exudative foci, whereas those slightly sensitive developed fine proliferative lesions. In China first infections will as a rule be small and will occur early in life, at which time it is known that skin (and so presumably tissue) hypersensitivity is not easily produced. Frequently repeated small reinfections will keep immunity high, but will at the same time act as desensitising inoculations. Unfortunately adequate quantitative tuberculin reactions are not available. Of 331 tests made in 1930 on Chinese adults of the artisan class, though 94 per cent. were positive, only three individuals showed a strong reaction, with vesiculation, to a dose of 0·1 mgm. (0·1 c.c. of dilution 1 : 1,000).

If it is true that tissue hypersensitivity is, in general, low in China, we see a further reason for lesions to be productive, non-toxic, and chronic; but if our hypothesis (that diminished sensitivity is the result of small infections frequently repeated) is correct, we must consider this also to be a result, and not the cause, of the chronicity of the lesions.

*Resistance.*—For the purpose of his theory Rich considers resistance to comprise the natural resistance of the human race to infection with the tubercle bacillus, *plus* the specific immunity acquired as the result of a prior infection, to the sum of which must be added or subtracted the variations above or below the average of human resistance which are found in individuals or races. This variable factor may be, in the individual, partly a fixed attribute connected with his constitution, and partly a fluctuating matter related to the state of his general health. In any given race it is considered to be a more fixed quantity which decides the tuberculous morbidity and mortality statistics for that race. Its existence as a genotypical racial attribute has been considered by many writers, and is called upon to explain particularly the difference in the type of tuberculosis seen in the negro and in the white population of the United States of America (Pinner[16]). History, however, tends to show that racial resistance is no fixed thing, and that within a given racial group the disease changes in morbidity and mortality in the course of years.

Neander[17] shows how in certain isolated rural areas of Sweden the disease changed from an acute malignant rapidly fatal type to assume a more chronic localising form, with a higher morbidity rate, but lower mortality. Anderson,[18] from a study of the disease in the island of Mauritius, shows how an isolated native population, when in continued contact with tuberculosis, begins to acquire resistance in thirty years, has acquired it to an appreciable extent in fifty years, and in more than one hundred and less than two hundred years has developed an immunity as high as that found in Europe. Brownlee[20] suggests that a considerable part of the decline in phthisis in England is in line with the " biological properties of diseases in general," and Coward[21] has drawn attention to the rarity of " galloping consumption " in England recently.

It is from evidence of this type that one is led to believe that the different types of tuberculosis seen in different races result, not from inherited differences in resistance to the disease, but from the length of time during which the race has had contact with the tubercle bacillus. Thus the acute, rapidly fatal tuberculosis seen by Borrel[19] in the French native troops during the war represents the reaction of any human population when first in contact with the tubercle bacillus. The reactions of South Africans,[14] Jamaicans,[13] and negroes[16] represent contacts over somewhat longer periods

of time. The reaction of Chinese, as described in this article, represents a contact considerably longer than that of the white races of the West. Any resistance, then, above the average of the human race as a whole is related to experience with the tubercle bacillus in point of time. This experience is considerably longer in China than elsewhere in the world, and so a study of the disease in China (where it has developed without any conscious effort at control) will reveal the most " adult," if not the ultimate, reaction of human tissues to infection with tubercle bacilli.

The fact that this ultimate working out of the fight between the bacillus and its human host leaves so much in favour of the bacillus should spur us all to renewed efforts in our attack on the disease, and demonstrate without reasonable doubt that the only hope of victory is along the line of complete eradication of the bacillus rather than in the direction of raising the resistance of the host.

In concluding, the author would like to emphasise that this article represents his own impressions after twelve years of clinical experience in North China. It is based on no careful analysis of statistics, but it is felt that the impressions conveyed are none the less accurate on that account. It is hoped that these impressions may stimulate an interest sufficient to suggest the importance of an effort to study tuberculosis in its more " adult " form, as the younger forms have been studied in South Africa and Jamaica. The public is becoming tuberculous-minded in China, and an Anti-tuberculosis Association has recently been formed in Shanghai. With economic factors so different and with a disease differing, no matter how slightly, from that seen in the West, an attempt to transplant anti-tuberculous measures, however successful they may have been in the country of their origin, and adapt them to Chinese conditions, would probably prove to be an expensive and largely unproductive experiment. The disease should be studied thoroughly in the economic environment in which it is found, and there will certainly develop measures directed toward its eradication which will probably differ considerably from any found suitable for its control in other countries.

**Summary.**

(1) Tuberculosis was known in China 2,600 years before the Christian era.

(2) Though no statistics are available, clinical experience shows that the disease is widely diffused through the population.

(3) Pulmonary tuberculosis occurs in a chronic non-toxic form with a long latent period.

(4) It is suggested that this tolerance of the disease represents, not a genotypical racial characteristic, but results from the long existence of tuberculosis in a static community.

(5) A detailed study of the disease in such an ancient civilisation would be well repaid, and would make an interesting contrast to those studies made recently of the disease in the younger races of South Africa and Jamaica.

## REFERENCES


1. Pan Dschi Kou: Beitrag zur Frage der Tuberkuloseverbreitung in China. *Beitr. z. Klin. d. Tuberk.*, 1933, **82**, 641-654.
2. Annual Report of the Shanghai Municipal Council, Public Health Department, 1933.
3. Chun, J. W. H.: Non-pulmonary Tuberculosis in China. *Nat. Med. Journ. of China*, 1928, **14**, 245-251.
4. Report of Roberts Memorial Hospital. *China Med. Journ.*, 1918, **32**, 487.
5. Heine, J.: Pathologisch-anatomische von Chinesen. *Tung-chi Med. Monatsschrift.*, 1932, **8**, 1-13.
6. Hall, G. A. M., and Chang, C. P.: Latent Infections in Chinese Adults. *Amer. Rev. Tuberc.*, 1934, **30**, 193-208.
7. Bumé, G. F.: Discussion of Paper by H. G. Anderson. *Chinese Med. Journ.*, 1934, **48**, 207.
8. Ku, Y., and Simon, M. A.: Experimental Amyloidosis. *Archives of Pathology*, 1934, **18**, 245-251.
9. Rich, A. R., and McCordock, H. A.: Pathogenesis of Human Tuberculosis. *Bull. Johns Hopkins Hosp.*, 1929, **44**, 275-423.
10. Smith, Theobald: Study of Bovine and Human Bacilli from Sputum. *Journ. Exp. Med.*, 1898, **3**, 451-511.
11. Saenz, A., and Costil, L.: Variantes dissociées de cultures de Bacilles tuberculeux. *Comptes Rendu Soc. de Biol.*, 1933, **114**, 1263-65.
12. Pinner, M.: Modern Concepts in Pathology. *Amer. Rev. Tuberc.*, 1928, **17**, 617-626.
13. Opie, E. L.: Tuberculosis in Jamaica. *Amer. Rev. Tuberc.*, 1930, **22**, 613-625.
    Opie, E. L., and Isaacs, E. J.: Tuberculosis in Jamaica. *Amer. Journ. Hygiene*, 1930, **12**, 1-61.
14. Tuberculosis in South African Natives. Publication of South African Institute for Medical Research, 1932, **5**, 1-429.
15. Shipman, S. J., and Davis, E. A.: Tuberculosis among Nurses. *Amer. Rev. Tuberc.*, 1933, **27**, 474-487.
16. Pinner, M., and Kasper, J. A.: Tuberculosis in American Negroes. *Amer. Rev. Tuberc.*, 1932, **26**, 463-491.
17. Neander, G.: The Dissemination of Tuberculosis in Sweden. *Acata Tuberc. Scandinavica*, 1928, **3**, 191-317.
18. Anderson, D. D.: Tuberculosis in Mauritius: Developed Resistance. *Trans. Roy. Soc. Trop. Med. and Hyg.*, 1928, **21**, 463-472.
19. Borrel, A.: Tuberculose chez les troupes noires. *Ann. de l'Inst. Pasteur*, 1920, **34**, 105-148.
20. Brownlee, J.: Epidemiology of Phthisis in Great Britain. Medical Research Committee, Special Report Series, No. 18, 1918.
21. Coward, N. A.: Annual Report of Medical Officer of Health for Leicestershire, 1929. Quoted by A. S. MacNalty: Report on Public Health and Medical Subjects, No. 64, 1932.

# DISTRIBUTION AND COMPARATIVE MORBID ANATOMY OF TUBERCULOSIS IN CAPTIVE ANIMALS

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## Zoological Distribution.

All orders of mammals, birds, reptiles, amphibians, and even fish, are liable, when kept in captivity or domestication, to contract an infection with acid-fast bacilli that cause in the tissues granulomatous inflammations or tubercles in which the specific bacilli can be demonstrated by the Ziehl-Neelsen method of staining. There is, however, a great difference in the degree of susceptibility of the various families and genera comprising an order of the animal kingdom. For instance, among Perissodactyla—in which Equidæ and Tapiridæ are included—tuberculosis is comparatively rare in mammals of the genus Equus. The disease is uncommon in the domestic horse. Calmette found only one case in 15,000 cab-horses examined in Paris. It was, and perhaps still is, more frequent in London horses; but among over 3,500 old decrepit horses slaughtered during the last ten years for feeding to carnivores in the London Zoo, no case of tuberculosis has been detected by veterinary inspection. Donkeys and mules are even more highly resistant, and it is stated that they do not acquire the disease naturally. I have seen no case of tuberculosis in any species of wild horse, ass or zebra, and, though the latter are very common menagerie animals, I can find only one case recorded in the literature.[1] Tuberculosis in horses is usually an abdominal disease, characterised by enlargement of mesenteric or cervical glands and large tuberculoma in liver and spleen. Among the Tapiridæ, however, both the existing species of tapirs are very susceptible to tuberculosis of the pulmonary type, and in captivity they commonly die from this. The Australian and American marsupials are relatively resistant; only a very few cases have been recorded in kangaroos and American opossums. In the order Artiodactyla, in which Cervidæ, Bovidæ, Suidæ and Camelidæ are included, the deer, antelope, oxen and pigs are perhaps the most susceptible of all mammals, whereas amongst camels remarkably few cases of tuberculosis have been recorded in India and Egypt where this common domestic animal must have ample opportunity of acquiring infection. Their American representatives the llamas, however, are commonly infected.

The only animal of economic importance that is commonly infected with avian tuberculosis is the domestic pig, and in the rare instances in

which man has become infected with the avian type it seems more likely that he got it from a pig than from a bird. Young calves are occasionally infected with avian tubercle, and Stanley Griffith has described a case of chronic infection of the udder of a goat with avian tubercle.[2]

In the London Zoo a kangaroo recently died with tuberculosis of the pancreas, from which Stanley Griffith isolated the avian type of bacillus. Reptilian tuberculosis is found in crocodiles, lizards, snakes and frogs. The tubercle bacillus of cold-blooded animals is not infective to mammals, so far as is known at present; and the susceptibility of birds to reptilian or amphibian tuberculosis is as yet unsettled.

Tuberculosis among animals living free in their natural habitat is extremely rare, but any species of wild deer, antelope or swine running free in parks or estates where cattle graze is readily infected from tuberculous domestic animals. Cases of natural infection have been reported, however, but they appear to have occurred only in *Mus musculus*, the common house-mouse, a species which in towns is almost a domesticated creature, often living in close association with infected humans, cattle or poultry.

The disease appears to be equally rare as a natural infection among wild birds. Perhaps the only genuine case is that recorded by Shattock in a wild lapwing (*Vanellus vanellus*) captured in Scotland, a species rarely kept captive. This specimen is now in the Museum of the College of Surgeons.[3] Hare, late pathologist at the Royal Veterinary College, recently described a case in a wild blackbird (*Turdus merula*) that was killed by a cat in a London garden, and may have escaped from captivity.[4] Another case in a kestrel hawk (*Falco tinnunculus*) recorded by Hammond Smith is open to the same possibility of having become infected whilst in captivity. I myself have examined several tuberculous so-called wild pheasants picked up dead on shooting estates, but in every case it was ascertained that they were hand-reared birds and probably infected from their foster-mothers—domestic hens. Wild partridges are occasionally infected in the same manner. It seems probable, therefore, that there is no tuberculosis under wholly natural conditions of life in which nature demands continuous 100 per cent. efficiency in all wild creatures permitted to enjoy her freedom, and when man was a roving wild animal living in small parties, hunting and gathering his sustenance in the wilderness, it is unlikely that he was a victim of this chronic debilitating disease.

Among primates the Pongidæ (the great apes), the Catarrhini (Old World monkeys), and the Platyrrhini (New World monkeys), are about equally susceptible to tuberculosis of human or bovine type, except the Lemuridæ (lemurs), which are lower in the scale and less susceptible. Gibbons and the Hapalidæ (marmosets) appear to be highly resistant, though the latter

are commonly kept in public menageries and privately as pets, and therefore presumably exposed to infection. I have searched the literature in vain for a record of tuberculosis in gibbons and marmosets, and though I have examined many of these animals during the last seven years, I have not yet found one infected with this disease. It may be noted also that certain manifestations of tuberculous infection, such as tuberculous disease of bones and joints, cutaneous tuberculosis, lupus and lichen scrophulosum, that occur in the human subject, do not appear to have been recorded among subhuman primates, possibly because the disease progresses so rapidly in these animals that they die before lesions can be recognised in the more resistant tissues. Some years ago tuberculosis was very prevalent among primates in the London Zoo and caused heavy losses, but since 1926 the incidence in apes and monkeys has been so reduced by sanitary methods that the disease now occurs only as an importation in newly-arrived animals. It is detected during their period of quarantine and the infected animals are destroyed. Among small wild animals that are often kept as pets in England the common hedgehog may be mentioned as one in which tuberculosis is not infrequent, and is probably acquired from eating tuberculous sputum or being fed on infected cow's milk.

Tuberculosis is widely distributed among all families of captive carnivora except hyænas and the pinnipedia (sea lions, walrus and seals), in which I can find no record of this disease.

The zoological distribution of cases of tuberculosis among mammals in the London Zoo during the last seven years is shown in Table I.

TABLE I.

| | *Cases.* |
|---|---|
| Pongidæ (gorilla, chimpanzee, and orang utan) .. | 4 |
| Catarrhini (Old World monkeys) .. .. .. | 9 |
| Platyrrhini (New World monkeys) .. .. .. | 5 |
| Bovidæ (oxen, antelope) .. .. .. .. .. | 20 |
| Cervidæ (deer) .. .. .. .. .. .. | 13 |
| Tapiridæ (tapirs) .. .. .. .. .. .. | 3 |
| Suidæ (swine) .. .. .. .. .. .. | 1 |
| Viverridæ (civets, mongoose) .. .. .. .. | 3 |
| Canidæ (dogs) .. .. .. .. .. .. | 2 |
| Petauristidæ (squirrels) .. .. .. .. .. | 1 |
| Macropodidæ (kangaroos) .. .. .. .. | 2 |
| Felidæ (tiger) .. .. .. .. .. .. | 1 |
| Ursidæ (bears) .. .. .. .. .. .. | 5 |
| Pteropodidæ (fruit bat) .. .. .. .. .. | 1 |
| Cuniculidæ (cavy) .. .. .. .. .. | 1 |
| Camelidæ (llamas) .. .. .. .. .. | 2 |
| Erinaceidæ (hedgehogs) .. .. .. .. .. | 1 |
| Procyonidæ (coatis) .. .. .. .. .. | 3 |
| Dasypodidæ (armadillo) .. .. .. .. .. | 1 |

For types of infecting bacilli in captive wild animals from the London Zoo see: "Isolation of Tubercle Bacilli from Captive Wild Animals." By R. Lovell. *Journal of Comparative Pathology and Therapeutics*, vol. xliii., Part 3, pp. 205-215, September, 1930. "Tuberculosis in Captive Wild Animals." By A. Stanley Griffith. *Journal of Hygiene*, vol. xxviii., No. 2, November 26, 1928.

I know of no bird that is not liable to infection with the avian type of tubercle bacillus when kept in captivity. It is possible, however, that among the 40,000 known species of birds at present in existence some may be immune. In the London Zoo, however, tuberculosis ranges through birds of all sorts and sizes, from ostriches to humming-birds. Gallinaceous birds, pigeons and ducks are most susceptible; flamingoes appear to be the least susceptible, and live for years in a crowded duck-pond in which there are tuberculous ducks. I myself have seen only one tuberculous flamingo, and I have examined many of these birds. With the exception of Cockatoos and parrots, birds are resistant to the human and bovine strains of tubercle bacilli, though in America human tubercle bacilli have been reported in gallinaceous birds and one case of bovine tubercle in a duck.[5]

**Morbid Anatomy and History.**

In nearly every case of tuberculosis in captive wild animals the primary lesion occurs in the lung or in the intestine, and is followed by secondary lesions in the lymph channels and lymphatic tissues; and in the most susceptible creatures, such as bovines and gallinaceous birds, general dissemination of the disease may be very rapid, and tuberculous foci may be found in almost every soft tissue of the body. Tuberculosis of bones is rare in captive wild animals, and is most likely to be met with in the spinal vertebræ of bovines. Tuberculous arthritis is not uncommon among gallinaceous birds, but I have not yet seen a tuberculous joint in a wild mammal. There is a general similarity in the gross and microscopic appearance of tuberculous lesions in all classes of animals, but they may vary in distribution and in their destructive effects according to the kind of animal infected. For instance, carnivora show an ulcerative type of the disease, and extensive pulmonary cavitation and gangrene is usual in tuberculosis of felines, but is uncommon in bovines, wherein caseating broncho-pneumonia and pulmonary consolidation with a plentiful distribution in the pleura of the characteristic firm, dense globular tubercles known as pearl nodes and caseous or fibro-calcareous masses of tuberculous lymph glands are the usual manifestations of pulmonary tuberculosis. The gross manifestations of disease caused by the tubercle bacilli in wild mammals may be confused with lesions caused by the various forms of pseudo-tuberculosis, caseous lymphadenitis, or with mycotic ulceration and deposits in mammals. Tuberculous deposits in the viscera of birds

or reptiles are sometimes quite indistinguishable from mycosis except by microscopic examination after Ziehl-Neelsen staining. Moreover, in birds and reptiles mycotic and tuberculous lesions may co-exist and can be demonstrated by the appropriate staining technique for moulds and for tubercle bacilli. In reptiles caseous helminth cysts may require microscopic examination to distinguish them from tubercles. In wild animals it is seldom possible to correlate tuberculous lesions found after death with any recognisable symptoms to which they may have given rise during life. Diagnosis depends upon microscopical examination of the lesions after death.

Tuberculous lesions in apes and monkeys as regards their pathologic anatomy and morbid histology are indistinguishable from those with which we are familiar in the lungs, intestines and lymphatic system of the young human subject.

In the primates the primary focus of infection undoubtedly occurs most frequently in the lungs, but whether the portal of entry is pulmonary or intestinal, the disease is invariably fatal in apes and monkeys, and so rapidly becomes generalised that it may be impossible to determine the original focus of infection.

Dr. Harold H. Scott, my predecessor in the pathological department of the London Zoological Gardens, published in 1930 an exhaustive comparative study of tuberculosis in man and the lower animals in which is embodied an anatomical paper by Scott and Beattie.[6] I will continue, therefore, with a few observations gathered from my own experience and study.

Just as the various manifestations of tuberculosis in apes and monkeys are almost identical in their pathologic anatomy and histology with those found in the human subject, so in the Bovidæ and Suidæ the lesions found in captive wild oxen, deer, antelope and swine closely resemble in character and localisation those described as commonly occurring in their respective domesticated representatives.

Tuberculosis of the uterus is not uncommon in domestic cattle and in captive wild Bovidæ, but I have not yet seen a case of congenital tuberculosis in a wild animal, though congenital tuberculosis of domestic calves is known to occur.

Tuberculosis in captive wild Bovidæ and swine can sometimes be diagnosed during life by the appearance of firm nodular tumours behind the angle of the mandible due to tuberculous enlargement of pharyngeal and cervical lymph glands, which soon break down and discharge through external sinuses. Infected animals should be destroyed and their carcases burnt as soon as the disease is diagnosed.

In tuberculosis of wild Canidæ the pericardium in nearly always seriously affected and distended with large quantities of serous or purulent exudate

in which tubercle bacilli are easily detected. Hydrothorax and ascites are also common complications in this family of carnivora.

The microscopic structures of the tubercle in different orders of mammals varies so little that in a mixed assortment of histological preparations from the mammalia it would be difficult to distinguish between human tubercles and those from other representatives of mammalian families. It may be stated, however, that bovine tubercles are more strongly constructed and usually show a more dense accumulation of histiocytes. The giant-cell system is common to all infected mammals that I have examined.

Bland Sutton, conducting pathological work in the London Zoological Gardens in 1881, was the first to bring avian tuberculosis under the notice of British pathologists. He diagnosed the disease in the Zoo on the naked-eye features of the lesions, and his diagnosis was confirmed in 1883 by his colleague Dr. Gibbs, who was skilled in the bacteriological technique of those days.

The *Bacillus tuberculosis avium* as seen in the tissues of birds is usually more slender and shorter; it is very variable, however, and sometimes quite long filamentous forms are observed. It tends, like the leprosy bacillus, to form dense clusters within the cells, and perhaps the most constant and striking feature in the distribution of avian tubercle bacilli is their partiality for the spleen, which they often convert into a large nodular or caseating tuberculoma in which no particle of splenic tissue can be recognised. Moreover, it is remarkable that birds of fine plumage, paradisea and equally gorgeous pheasants will die in extreme emaciation from generalised tuberculosis in the full beauty and colour of their resplendent nuptial plumes.

The liver and kidneys of birds are not infrequently destroyed by tubercles. When the kidneys are infected, the urinary tubules are found distended with masses of tubercle bacilli, in which case there is ample reason to believe that conjugal infection occurs between cocks and hens occupying the same run. Tuberculosis of the ovary is frequent, especially among ducks and other water-fowl; for instance, a gallinule (*Porphyrula martinicus*), a kind of water-hen, died from pressure effects of an ovarian tumour the size of a hen's egg. On section the tumour was found to be an overgrown and inspissated egg yolk in which masses of tubercle bacilli in pure culture were growing in a natural egg medium! The only other lesions were a few miliary tubercles in the spleen. A particularly virulent form of intestinal tuberculosis occurs among gallinaceous birds in which an acute hæmorrhagic enteritis is the only lesion visible to the naked eye. Microscopical examination of a smear of the intestinal contents reveals what appear to be a pure culture of tubercle bacilli. Sections of the gut show colonies of bacilli in the solitary follicles and the

epithelial cells of the mucosa packed with acid-fast bacilli. Such cases are a great danger in the poultry-run or aviary, since in birds the intestinal mucosa is the most common portal of infection whereby the tubercle bacilli can enter, and leave no trace. Once in the venous circulation, the bacilli colonise in the liver and spleen, which are quickly destroyed by an agglomeration of tubercles.

In respiratory tuberculosis of birds it is not uncommon to find the disease localised in the trachea and syrinx, the mucosa of which is destroyed and replaced by a caseous exudate swarming with acid-fast bacilli in pure culture. In such cases the lymph channels along each side of the bird's neck may form a chain of enlarged tuberculous lymph nodes homologous to the chain of enlarged tuberculous cervical glands met with in certain cases of tuberculosis in mammals. The histological feature of the avian tubercle is rapid centrifugal extension of the growth of epithelioid cells, the intracellular concentration of the bacilli in this area, and the early and advancing necrosis of the interior of the tuberculous focus. Giant cells are generally absent, and if present are not characteristic, since they occur also around mycotic foci in birds. In the muscles of birds, and sometimes in their air sacs or lungs, the tubercles may be enclosed in a fibrous capsule, but in the latter situation pulmonary gangrene is more frequent.

Reptilian and amphibian tuberculosis may be pulmonary, alimentary or generalised. The bacilli vary greatly in length and breadth; some are long, stout and filamentous-like leptothrix threads, others are short, slender, segmented and approximate more towards the avian type of bacilli. Crocodiles, lizards, snakes and frogs are affected in about equal proportions.

The lesions in alimentary infections are intestinal ulceration and hard dense tuberculous nodules in the submucosa, mesentery, liver and spleen. If the lungs are affected, the tubercles are usually soft and caseous; but in the tissue immediately adjacent to the lung, hard nodular tubercles are found. Reptilian and amphibian tubercles are usually enclosed in a capsule of fibrous tissue, soft and œdematous in pulmonary lesions, firm and dense elsewhere. They all show central necrosis, but no giant cells. They are indistinguishable from mycetomatous deposits except by appropriate staining and microscopical examination.

## REFERENCES

1. Fox, Herbert: Diseases in Captive Wild Animals and Birds, p. 501.
2. Griffith, A. S.: *Journal of Comparative Pathology and Bacteriology*, 1931, vol. liv., Part 2, pp. 144-148.
3. Cobbett, L.: The Causes of Tuberculosis (Cambridge University Press), p. 527.
4. Hare, Tom: *Proceedings Royal Society Medicine*, vol. xxv., No. 10.
5. Fox, Herbert: *Proceedings United States Live Stock Association*, 1924.
6. Scott, H. H.: Tuberculosis in Man and Lower Animals. Medical Research Council Special Report Series, No. 149.

# THE B.C.G. VACCINE AND ITS PRACTICAL APPLICATION

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I HAVE been invited to give a practical account of the present position of the B.C.G. vaccine, and of its application in this country. The B.C.G. vaccine is a suspension of living attenuated tubercle bacilli; the original strain was a virulent bovine bacillus which was grown by Calmette and Guérin on a glycerine-bile-potato medium until it had lost all virulence for laboratory animals. At this point Calmette declared that it had become a "virus fixe" and gave it the name "B.C.G." (Bacille Calmette-Guérin); he directed, however, that it should only be grown on glycerine-potato and should still be returned to glycerine-bile-potato at every tenth subculture.

The protective action of the vaccine is due to "Koch's phenomenon"—the fact that a guinea-pig already infected with a weak strain of the tubercle bacillus is refractory to a second infection, and though the primary infection slowly runs its natural course and ultimately kills the animal, the secondary infection after producing a local reaction rapidly heals. Calmette argued that if a strain could be attenuated so that it could not produce progressive tuberculosis, but would still produce an immunity, then an animal primarily infected with this innocuous strain would become resistant to any subsequent virulent infection.

That Koch's phenomenon also occurs in man is generally accepted, and it is safe to say that—all other things being equal—the man who already harbours tubercle bacilli in his body is more resistant to a tuberculous infection than is the man who becomes infected for the first time. This is borne out in practice by Heimbeck's work;[1] he showed that the morbidity rate from tuberculosis of pupil nurses at his hospital was 2·6 per cent. for those who were Pirquet-positive on arrival, and 29·6 per cent. for the Pirquet-negative. It is for this reason that the primary or childish form of tuberculosis is so much more readily contracted than the secondary or adult form, and may so rapidly become generalised. Calmette postulated that if all children were infected with an apathogenic strain at birth, their resistance would be raised and the infant mortality rate from tuberculosis would rapidly fall.

With this end in view Guérin began to experiment with cattle, and succeeded in protecting a large proportion of the calves in a tuberculous herd;

Calmette obtained correspondingly successful results with laboratory animals; and in 1922 Weill-Hallé ventured to give the vaccine to children. The early reports showed extremely encouraging statistics and the vaccine became in great demand in France.

During this time England had maintained a conservative attitude, especially as the vaccine was an emulsion of living bacilli and so carried with it the theoretical danger of infecting the child with tuberculosis. This attitude seemed more than ever justified when in 1927 Petroff[2] published a paper showing than on gentian-violet-egg it was possible to dissociate the culture into an " S " and an " R " type, and that the " S " type was virulent for guinea-pigs. The reports of other investigators increased the mistrust felt in England, and the final blow was dealt in 1930 by the disaster at Lübeck. In this catastrophe seventy-three children who had been given the vaccine in the spring died before the end of the year.

But instead of the B.C.G. vaccine falling into disuse, as was predicted in this country, after a temporary check its use became more widespread than ever; today nearly a million and a half children have been inoculated in clinics from Sweden to Indo-China. England is one of the few countries left in which there is no active interest taken in the vaccine.

It was for this reason that during my tenure of the Radcliffe Travelling Fellowship I visited as many B.C.G. laboratories and clinics in Europe and America as possible in an attempt to review the position impartially. The two main problems are:

1. Is the B.C.G. vaccine safe to give to children ?
2. Does it produce any immunity ?

I shall only go briefly into the question of the return of virulence in cultures and animals; the evidence has been discussed in detail elsewhere.[3] There is little doubt that Petroff and others have dissociated a virulent variant from the B.C.G. by growing it on special media; consequently, Calmette was wrong in describing the B.C.G. as a " virus fixe." On the other hand, this dissociation into " S " and " R " types does not occur when the culture is grown in accordance with Calmette's instructions, so that this objection is of more academic than practical interest; even Jenner's vaccine can be altered by cultural methods.

Of greater importance is the fact that a certain number of investigators have succeeded in producing tuberculosis in guinea-pigs by inoculating them with B.C.G. Some of the earlier results may be discredited because the investigators did not realise that the vaccine may temporarily produce a typical tubercular pathology, which is, however, benign and retrogressive; but the extensive work of Watson[4] and of Petroff[5] leaves little doubt that

their animals at any rate developed genuine tuberculosis. Nevertheless, in fairness to its supporters it should be remembered that the guinea-pig is considerably more susceptible to tuberculosis than is the average infant.

An interesting fact arises in connection with these experiments. Though virulent dissociation and virulence for guinea-pigs was demonstrated with comparative ease in 1928, later investigators have found increasing difficulty in reproducing these results. If we accept Petroff's hypothesis that there are two strains in the B.C.G., an avirulent " R " and a virulent " S," these later failures are capable of explanation. Bile-glycerine-potato is an unfavourable medium for the growth of the " S " type, and so by repeated subculturing on this medium the virulent element has been continually reduced and the avirulent " R " type has been encouraged. Consequently, though in 1928 there was still sufficient of the " S " type to revive and prove fatal when suitably grown, in subsequent years its steady decrease has made the repetition of these experiments increasingly difficult.

The question then arises as to how much any immunising property of the vaccine may be due to the trace of the virulent type that still remains. If this trace is the important factor, the future criticism of the vaccine may be not that it is dangerous, but that it is so harmless as to be useless; this does not concern us as yet.

But these arguments as to the possible return of virulence *in vitro* and in animals are of interest only to those who first dared to apply the vaccine to infants. With a million and a half children already inoculated there is ample material for a much more direct investigation of the safety of the B.C.G. for man.

In weighing the evidence it must be clearly understood that the vaccine does not claim to give absolute protection from tuberculosis, and therefore a certain number of inoculated children, if exposed to infection, will inevitably die from typical tuberculosis. The literature contains several reports of inoculated children living with tuberculous parents who have died from tuberculosis, in which no investigation and no autopsy was performed, and yet the case is published as a proof of the danger of the vaccine.

The disaster at Lübeck is so notorious that it has even brought the topic into the lay press. The following is a brief summary of the tragedy:

A culture of the B.C.G. was obtained from Paris by Deycke of Lübeck, who, contrary to Calmette's instructions, grew it on an egg medium before using it to make the vaccine. In the same laboratory was a virulent culture from Kiel. The vaccine was prepared by Deycke and given to children in Lübeck; within a year seventy-three of the inoculated children had died from tuberculosis.

At an official enquiry it was clearly shown from the post-mortem evidence

that the source of the tuberculosis was the vaccine, and not accidental infection. Friedberger[6] summed the position up by pointing out that there were four possibilities:

1. The vaccine was contaminated with virulent bacilli.
2. The vaccine had become virulent in susceptible children.
3. The original culture from Paris had been virulent.
4. The culture had become virulent by growing it on an egg medium.

The last three possibilities can be individually disproved,[3] but it is sufficient here to show that the first hypothesis can have been the only possible explanation for the following reason: The Kiel culture, which was admittedly in the same laboratory at the same time, when grown in bouillon produced a definite green colour. Though this is not a unique characteristic, it is sufficiently uncommon to be distinctive; moreover, the B.C.G. has never been known to produce this change in bouillon. The incriminating fact is that the culture grown from the autopsy material produced this same green coloration. The laboratory stock of vaccine was, for some unknown reason, destroyed before the investigation took place, but a few ampoules were discovered and cultured; the green colour was again produced. On this evidence the court decided that a contamination from the Kiel culture had taken place, and that no blame was to be attached to the B.C.G.

Apart from Lübeck, there are only twenty to thirty deaths attributed to the vaccine in the whole of the literature. Of these, some are so poorly investigated as to be useless, and in the majority the child had been exposed to open tuberculosis; it is a striking fact that there is not one fatal case that has been proved beyond reasonable doubt to be due to the vaccine.

On the other hand, well over four hundred autopsies on B.C.G. children have been reported, and in no case have there been any signs of tuberculosis resulting from the vaccine.

Taking into consideration the large number of children who have already received the vaccine, there seems to be little evidence to suggest that the theoretical danger of a living vaccine has any significance in practice.

Turning next to the question of the amount of immunity produced by the vaccine, we are faced by almost insuperable difficulties. Two main methods have been attempted to evaluate the effects of the vaccine, which may for convenience be termed the " mass inoculation " and the " clinic " methods. In the former large numbers of infants are inoculated and an attempt is made to find out how many eventually die from tuberculosis; this figure is compared with the mortality figures for uninoculated infants.

The method is obviously crude, as many cases are untraceable and the number of autopsies performed to establish the cause of death are negligible. By the latter method all children in tuberculous families are watched in a clinic; half of them receive the vaccine, the remainder are kept as controls, and any deaths are autopsied.

Clearly the " clinic " is the method of choice, but even here the difficulty of obtaining true statistics are far greater than would at first be apparent. For instance, in Park's clinic in New York it was noticed that it was the more intelligent and careful mother who consented to the inoculation, and who at the same time carried out hygienic precautions better than the mother of the control infant; thus the conditions were biased in favour of the B.C.G. child. Again, a long time must elapse before sufficient cases have passed through the clinic to produce any figures. When I left New York seventy-eight children in Park's clinic had received the vaccine; one child had died in this time and at autopsy had shown no tuberculosis. Even if there were to be one death from tuberculosis in every 200 cases, it would need about 5,000 B.C.G. infants and 5,000 controls to produce any reliable statistics.

At the present moment we have to be content with a general survey of the rather doubtful figures reported by various clinics; it is clearly impossible to attempt to gauge the degree of immunity conferred, and we must confine ourselves to the simple question: Does the B.C.G. produce any immunity at all ?

Over 100 different clinics have published their results, and in practically every case some degree of protection has been reported. These reports come from such widely separated places as Italy, Uruguay, Japan, Algeria, and Madagascar, to name only a few. Wallgren[7] of Sweden has been giving the vaccine to exposed children in Göteborg. Before he began the infant death-rate from tuberculosis in Göteborg was 3·4 per 1,000; since then it has dropped to 1·4 (1928-32), and in 1933 it had reached the figure 0·3. In Oslo a large number of pupil nurses are drawn from isolated country districts, and in 1925 Heimbeck[1] found that half his probationers were Mantoux-negative; of these, 29·6 per cent. contracted tuberculosis in hospital. Later he began to inoculate all Mantoux-negative nurses with the vaccine, and in 1927 the tuberculosis morbidity rate in the B.C.G. group was 2·3 per cent.

From this we may safely conclude that the vaccine does evoke immunity; it will be several years before the actual degree can be worked out. To attempt to replace our present organisation for the prevention of tuberculosis by a wholesale inoculation of infants after the manner of Jenner's vaccination is unjustified on the incomplete evidence before us; we are therefore right in maintaining our conservative attitude as far as that is concerned. But in our fight against tuberculosis any factor that can give us the smallest

help is welcome; if, then, we can use the B.C.G. as an *additional* factor to the present scheme, surely we should not hesitate?

That there are many occasions on which it would be of assistance is known only too well to the general practitioner and the tuberculosis officer. Take, for instance, the case where the father in a small cottage is found to be suffering from tuberculosis. He is sent to a sanatorium for a few months; the mother and three young children are examined as contacts; nothing is found and the children are Mantoux-negative. Later the father returns from the sanatorium, arrested, and capable of doing four hours work a day; such work is practically unobtainable, and he either does nothing or eight hours. In the latter case sooner or later he breaks down again and exposes three young Mantoux-negative children to his positive sputum.

Surely we are wrong in our conservative attitude towards the vaccine in a case like this; anything that will increase the immunity of those children in however small a degree is valuable. For this reason I am going to give practical details of the administration of the vaccine, so that those health authorities and general practitioners who agree that there is a definite place for the B.C.G. in our present scheme may have some idea of the method of its administration.

At the present moment the vaccine cannot be obtained in this country, but the question of a suitable source of supply will, I hope, shortly be solved.

The vaccine is issued in glass ampoules, which must be ordered fresh, as it is not safe to assume that the B.C.G. is still alive after the tenth day. It may be given by mouth, subcutaneously, or intradermally. The French favour the first method, largely because of its simplicity, but recent work has shown—as might have been expected—that the results are far from uniform, as there is no regulation of the amount absorbed from the stomach. Subcutaneously the vaccine is much more even in its effects, but there is an unfortunate tendency to a sterile abscess, which, though harmless, is rather a deterrent to other parents. The intradermal method may sometimes produce a small ulcer about a fortnight after inoculation, which lasts for a few weeks; there is no general reaction, and in no case is the local reaction as severe as the average vaccination pustule. The local glands sometimes become enlarged, but the swelling is painless.

The vaccine is only to be used on Mantoux-negative children. If a child is Mantoux-positive it is an indication that it has already received a primary dose of tubercle bacilli, and will consequently show Koch's phenomenon on subsequent reinfection; the injection of the B.C.G. is therefore unnecessary and undesirable.

A positive Mantoux may take as much as six weeks to develop after infection; therefore the child must be isolated from the tuberculous member

for this period before the Mantoux test is performed. The vaccine is then injected into all Mantoux-negative children, and a further six weeks of isolation must elapse for the immunity to develop.

This would at first sight appear to be a somewhat complicated procedure, but it will be found to work out quite simply in practice. Let us suppose that the father in a working family is found to be suffering from open tuberculosis. In the normal course of events he is reported to the tuberculosis officer, who sends him to a sanatorium; the only proviso necessary in this case is that he should be kept away from home for a minimal period of three months. The mother and children are examined as contacts, and if nothing is discovered the mother is told to bring the children back in six weeks' time; this constitutes the necessary isolation for any late infected child to become Mantoux-positive.

At the end of this time the children are given 0·2 mg. O.T. intradermally into the forearm as a Mantoux test, and this is read in forty-eight hours (a health visitor could easily be trained to do this in the home); if the Mantoux is negative, they are brought up the following week and another test is made for safety's sake with 2·0 mg. O.T. If this also is negative, the child is again brought up at the end of a week, and a single injection of 0·05 mg. B.C.G. is injected intradermally into the middle of the outer aspect of the thigh. The child then returns home, and as the father is still due to be absent for at least six more weeks the immunity has the necessary time to develop while the child is isolated from infection.

Any babies born into the family should be notified to the tuberculosis officer at once, and should be inoculated within the first fortnight of life; preliminary Mantoux testing is, of course, unnecessary in these cases. The baby must then be kept from any contact with the father for six weeks.

I fully realise that purists will criticise me on several points, such as not Mantoux-testing the child again after inoculation to make sure that its immunity has been properly established. I agree that the method that I have outlined is not theoretically perfect. I have deliberately cut the performance down to its simplest form, so that the tuberculosis officer or general practitioner may not be put off by too elaborate a proceeding, and at the same time I do not believe that I have materially detracted from its effectiveness.

In conclusion I should like to say that, though the immediate use of the vaccine in tuberculosis clinics is my principal suggestion, it is difficult to see why we should not contribute to the estimation of the degree of immunity evoked. A clinic run in connection with a large hospital would not only help to elucidate the problem, but could also supply this country with the B.C.G. vaccine.

REFERENCES

1. HEIMBECK, J.: *Ann. Inst. Pasteur*, 1929, xliii. 1229.
2. PETROFF, S., BRANCH, A., AND STEENKEN, W., JR.: *Proc. Soc. Exper. Biol. and Med.*, 1927-28, xxv. 14.
3. IRVINE, K. NEVILLE: The B.C.G. Vaccine. Oxford University Press, London, 1934.
4. WATSON, E , MCINTOSH, C., AND KONST, H.: *J. Am. Vet. M.A.*, 1928, lxxiii. 799.
5. PETROFF, S.: *Am. Rev. Tuberc.*, 1929, xix. 9.
6. FRIEDBERGER, E.: *Deutsche med. Wchnschr.*, 1930, lxvi, 1300.
7. WALLGREN, A.: *J.A.M.A.*, 1934, ciii. 1341.

# SOME REFLECTIONS ON THORACOPLASTY

BY W. JULLIEN AND F. CH. ECOT

(From Pau.)

ALL active methods used in the fight against pulmonary tuberculosis during the last thirty years have been dominated by collapsotherapy. In spite of the most violent attacks on it pneumothorax prevailed, and its use on a large scale has logically led to lung surgery.

Generally the indications for the two methods are similar, with this important difference, that while Forlanini's method is usually temporary in its effects, thoracoplasty creates a permanent condition, and it is therefore evident that the pros and cons for the latter must be carefully thought out.

The early disasters—high mortality or chronic invalidism—following the operation were due to a lack of care in the choice of suitable cases or to an excessive interference with healthy tissue.

Partial thoracoplasty has made the operation one more readily accepted by the patient, giving rise to less shock and to less mutilation, and wherever possible it is to be preferred. However, where an extensive operation is unavoidable this should not be undertaken at once, but in different stages, thus avoiding grave risks and allowing a progressive and complete collapse of the lung.

Before giving some details of the operative technique we generally use it is necessary to state the indications for thoracoplasty. While Forlanini's method is used in active febrile conditions, lung surgery should only be applied in quiescent afebrile cases.

The relative merits of pneumothorax and thoracoplasty have been much discussed. A fairly long experience has led us to the definite conclusion that artificial pneumothorax is the most logical and efficacious weapon we have in the fight against pulmonary tuberculosis. Lung surgery has arisen

from those cases, such as pleural symphysis, where pneumothorax is impossible or inapplicable.

Firstly, we would say that we have to deal with unilateral, ulcerated, and definitely tuberculous lesions. But we would not reject cases of bilateral affections predominating on one side, the lesions on the other being quiescent, of no great extent, and showing radiological rather than clinical signs. As happens in certain pneumothorax cases, a successful operation may have the most beneficial effect on the other lung and help its healing. We must insist on the necessity for complete study of each case, both clinically and by the fluoroscope. This is indispensable. This is the only way to enable one to have an exact picture of the lesions both in extent and character. It necessitates, of course, an examination made from every angle to get the best radiographic result.

After getting all the information possible from every line of enquiry and examination, one can then decide on a line of procedure: whether to do the operation all at once or in several stages, how many ribs to resect and what length of each rib to remove.

On young and vigorous subjects seven ribs may be resected in a first stage—more often five or six, or even less in elderly or feeble patients.

According to the localisation of the lesion as shown by radiography, the operation will be carried out either posteriorly—in which case, if advisable, the transverse processes may be removed (Maurer)—laterally, or anteriorly.

It must also be borne in mind that while not interfering unnecessarily with healthy lung tissue, one must go beyond the actually diseased zone by resecting one or two ribs beyond this, remembering, too, that in women and children lung collapse is easier and quicker than in men or older people.

### Operative Technique.

We have always used local anæsthesia, the methods of which are now so perfected that they can be thoroughly relied on.

First, an intradermic infiltration at least ½ inch wide along the line of incision. Next, a broader infiltration of the underlying muscular layers, and generally at the same time the suprascapular nerve can be anæsthetised, which helps the raising of the scapula during the operation. Finally, anæsthetise the intercostal nerves. We have never found a patient unwilling to undergo further intervention after a first local anæsthesia owing to pain.

Ordinary paravertebral thoracoplasty easily permits the resection of the necessary ribs. We generally remove the whole of the first two and a large part of the others.

The incision we use begins exactly on the level of the spine of the scapula, and, equidistant from its vertebral border and the spino-apophyseal line, it is brought down parallel to the vertebral border of the scapula round its inferior angle and then outwards. The limits of the incision will, of course, vary with the number of ribs to be resected and with the muscular development of the patient.

The operation is carried out from below upwards, and if the lung collapses readily it gives one plenty of room and the work is extremely easy. When, however, pulmonary elasticity has been lost one gets a resistant layer of tissue which causes bulging of the intercostal space after the resection of each rib and makes access to the higher ribs more difficult. All the ribs being resected, there is no more to do than control the hæmorrhage, put a perforated drainage tube into the wound, bringing it out by a counter-incision made as low down as possible, join the muscular layers that have been cut, and stitch the skin with horsehair. An ordinary dressing kept in place by adhesive plaster is then put on.

**Pre- and Post-Operative Care.**

On the evening before the operation the patient should take a light supper and be given a little "Somnifène" before settling down for the night. This dose should be repeated the following morning and a hypodermic injection of "Sédol" given before he is brought into the operating room.

After the operation the patient is brought back to bed and placed in a half-sitting position slightly leaning over to the affected side. Drainage is effected by means of an india-rubber tubing led into a graduated glass half filled with some antiseptic solution. In this way the dressing is not soiled and the exudation can be measured. This usually amounts to 100 to 250 c.c. The drain can be removed after three or four days. We also give as a routine a glucose solution per rectum and such heart tonics or sedatives as may be called for. Generally there is no dyspnœa. Fever rises sometimes to 100·4° or 101·3° during forty-eight hours, and drops very quickly to normal, often more rapidly than after the simplest appendix operation. The stitches are removed on the tenth day.

We examine all our patients by fluoroscope on the fifth or seventh day and a radiograph is taken every fortnight. This is the best guide, showing the work done and what remains to be done.

If, as it is usually the rule, the results are normal, the second stage must be done after two or three weeks, bearing in mind that the quicker one goes the more chances one has to get a perfect healing. When the patient is too tired or when complications occur (suppuration, congestive attack), it is necessary to wait.

### Secondary Stages.

The usual paravertebral thoracoplasty generally allows the removal of the six or seven first ribs. But if it is intended to make a total thoracoplasty, a second stage is required, this time inferior, which allows the resection from the sixth or seventh to the tenth rib included. The technique is the same as above described, except that the ribs are reached by a lower incision. Special indications may necessitate certain modifications; thus a large cavity of the apex, especially if posterior, may require the resection of transverse processes (Maurer), whilst, on the contrary, an ulceration in the front part of the lung will necessitate an anterior operation. If it is intended to remove the anterior part of the ribs as far as the costal cartilages, but not including them, the axillary route is perfect. But if the costal cartilages have also to be removed, the para-sternal route must be employed.

The secondary operations are easy to carry out if performed soon after the initial stage. If for any reason it becomes necessary to operate long after the first stage, one meets with the extreme difficulty caused by bony new formations. The ribs very seldom regenerate in their original form. Their shape, their surprising prominences, the bony bridges they throw on their neighbours, their variable consistency, make it practically impossible to apply the usual technique; local anæsthesia becomes almost impossible; abnormal ribs are not easy to take hold of and to free; their deep surfaces are very delicate, since the pleura adapts itself closely to their irregularities.

### Thoracoplasty and Artificial Paralysis of Diaphragm.

Phrenic resection is no longer systematically associated with thoracoplasty as formerly. Experience has taught us to think of the future, and we have often regretted having definitely paralysed a diaphragm.

For our part we apply phrenicectomy only in cases of lesions affecting the whole lung and when there is no hope of the base becoming useful. When the upper lobe alone is affected, we have given up the removal of the nerve and prefer treatment by injection of alcohol. Varying the proportion of alcohol absolute, 90°, 80°, 70°, it becomes almost possible to direct the duration of nerve inhibition.

### Incomplete Pneumothorax and Thoracoplasty.

When pneumothorax is incomplete, with apical symphysis, and not effective on account of a cavity remaining open, total thoracoplasty is not necessary if the lesion is limited. Courcoux and Bernou have published

wonderful cases treated by partial thoracoplasty, after which pneumothorax was kept on regularly. We ourselves have cases which prove this.

Two things must be remembered: first, the necessity of extracting gas before the operation, to prevent sudden over-pressure capable of disturbing the patient; secondly, the great care the surgeon must take during the operation lest he should tear the pleura, at this place very thin and non-adhesive.

**Complications.**

Complications of course do occur, but very seldom. We must mention the fatal accidents during the three or four days following the operation—heart collapse, meningitis, abrupt spread to healthy parts by sudden expression of the infected apex. These are recollections of old times and ought to disappear. More frequent are the wall suppurations, usually of no gravity, and the congestive attacks.

They may occur in the very place where the operation has been made, in consequence of a special sensibility of the lung reacting to the slightest traumatism; at the base of the lung on the same side; or in the opposite lung. Careful choice of patients usually prevents all serious accidents, or at most reduces their incidence. It is precisely in those cases that extra treatment such as gold may be of great use.

All our patients have been operated on at the sanatorium under excellent conditions, since they changed neither their society nor their habits, and all the operations have been preceded and followed by hygienic dietetic treatment and long rest in bed.

We would also stress the fact that fortunately we worked in a station of low altitude, of high barometrical pressure, especially suited to seriously affected patients, who thus have had a great advantage.

But we are certain that we owe the major part of our success to the fact that such operations were decided upon and carried out with the most intimate and loyal collaboration of physician and patient, and therein, we believe, lies the real secret of success.

# THE VALUE OF THE TRIBOULET REACTION IN INTESTINAL TUBERCULOSIS

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An account of Triboulet's test for intestinal ulceration in a recent number of the *British Medical Journal* encouraged us to investigate the reaction with a view to determining the advisability of adopting the test as a routine adjunct to the physical examination of the phthisical patient.

Being impressed by the fact that a considerable number of fatal cases of pulmonary tuberculosis show evidence of intestinal ulceration, usually some months before death, we felt that some evidence of intestinal infection at an incipient stage would be of prognostic value. In the hope of diagnosing intestinal ulceration at this stage we utilised Triboulet's reaction and have performed this test on 109 cases.

### Method of Performing the Test.

A lump of fæces as large as a walnut is dissolved in 20 c.c. of distilled water and filtered; 3 c.c. of the filtrate is diluted with 12 c.c. of distilled water; 20 minims of Triboulet's reagent (sublimate 3·5, acetic acid 1, aqua dest. ad 100) are added. As a control the same filtrate is used without Triboulet's reagent. The test tubes containing the two solutions are well shaken, and are compared after five and twenty-four hours. A positive reaction is indicated by a cloudy grey or brown deposit, above which the solution is clear.

### Biochemical Notes.

1. Albumen and globulin were detected in the fæcal filtrates. Both these proteins are precipitated by the reagent.

2. The ratio of the albumen and globulin present in the filtrates was examined in 46 cases. This ratio showed wide variations, ranging from 1·18 to 24·0. There was no definite relationship between the ratio and the

type of reaction, except that in the strong reactions (++ 5 hours) the proportion of albumen tended to be high.

3. Alteration of the concentration of the fæcal filtrate has little effect on the rate of precipitation, but modifies the degree of precipitation in proportion to the dilution (1/1, 1/2, 1/4).

4. The effect of the reagent on diluted blood serum was tested. Up to dilutions of 1 : 5 a positive reaction results. In greater dilutions the reaction is negative. Specimens of albuminuria and solutions of dilute egg white gave similar results.

5. The fæces were repeatedly examined for occult blood by the benzidine test. The presence or absence of blood has apparently no influence on the reaction, presumably because the concentration never reaches the critical value of 1 : 5.

6. It is reported that, as a result of decomposition of the proteins, specimens of fæces obtained at post-mortem give negative reactions, although during life the reactions may have been positive. We have failed, with the exception of the one case quoted below, which gave a dual reaction, to observe this phenomenon in the 16 post-mortem cases examined. Fifteen of these gave positive reactions, irrespective of the post-mortem condition; only one post-mortem specimen gave negative reactions, but the reaction was also negative during life. Further to investigate the point we kept specimens of fæces for a period of four weeks, ample time to permit of decomposition. These were examined weekly. In every instance the reaction remained as at the commencement and, if anything, became slightly more marked as time advanced.

7. It is known that in intestinal tuberculosis fæcal nitrogen excretion is considerably increased, and that an early sign of this infection is a drop in the total blood proteins as determined by refractometry.

With a view to finding a possible connection between these factors and the Triboulet reaction, we compared in 21 cases the albumen globulin ratios of the fæcal filtrate with the albumen globulin ratio of the blood serum. It was thought that the lowered blood protein might be the outcome of secretion from intestinal ulcers, and that a study of the respective albumen and globulin ratios of the fæces and blood might enable one to establish the origin of the intestinal protein as a transudate from the blood fluids. No such correlation could be traced. This investigation was undertaken on the assumption that the Triboulet reaction is a true index of the intestinal condition, an assumption which the later analysis of our results showed to be unwarranted. The findings cannot therefore be regarded as significant proof one way or the other of the site of origin of the proteins which give rise to the Triboulet reaction (see Table III.).

At the commencement we realised that any clinical classification must be arbitrary, chiefly because it rested very largely on a symptomatic basis.

From the point of view of investigating the test we agreed upon the following classification:

1. *Clinically Definite.*—All those cases in which there was more or less constant abdominal tenderness and pain, nausea and intermittent constipation and diarrhœa.

2. *Clinically Probable.*—Those in which there occurred periodic attacks of abdominal pain, sometimes accompanied by vomiting and diarrhœa, and associated with a greater loss of weight than one would have expected from the pulmonary lesions alone.

3. *Clinically Negative.*—All other cases were classed as negative.

In every case the test was carried out without any knowledge of the clinical condition, and it was only at the end of the investigation that results were compared.

TABLE I.

93 *Clinical Cases :*

| | | | |
|---|---|---|---|
| Agreement .. .. .. | 37 = {T+, C+ = 22 / T−, C− = 15} | 39·8 per cent. |
| Disagreement .. .. .. | 56 = {T+, C− = 52 / T−, C+ = 4} | 60·2 per cent. |

8 *Cases, P.M. only* (Fæces examined P.M.):

| | | | |
|---|---|---|---|
| Agreement .. .. .. | 3 = {T+, P.M. + = 3 / T−, P.M. − = 0} | 37·5 per cent. |
| Disagreement .. .. .. | 5 = {T+, P.M. − = 5 / T−, P.M. + = 0} | 62·5 per cent. |

8 *Cases examined Ante-mortem and Post-mortem :*

| | | | |
|---|---|---|---|
| Agreement .. .. .. | 7 = {Intestinal + = 6 / Intestinal − = 1} | 87·5 per cent. |
| Disagreement .. .. .. | 1 = {P.M. − C, − / T.P.M. + T, +} | 12·5 per cent. |

TABLE II.

ANALYSIS OF 93 CLINICAL CASES.

| | *Clinically.* | | |
|---|---|---|---|
| | *Negative.* | *Probable.* | *Positive.* |
| Triboulet − .. .. .. | 15 | 3 | 1 |
| Triboulet + (5 hours) .. .. | 34 | 8 | 7 |
| Triboulet + (24 hours) .. .. | 18 | 7 | 0 |

TABLE III.

| *Case No.* | *Protein in Fæces.* | | *Protein in Serum.* | | *Triboulet Test.* | *Clinical Findings.* |
|---|---|---|---|---|---|---|
| | A : G. | A/G. | A : G. | A/G. | | |
| 4 | 78 : 22 | 3·55 | 52 : 48 | 1·08 | − | + |
| 5 | 82 : 18 | 4·55 | 52 : 48 | 1·08 | + | + |
| 7 | 65 : 35 | 1·7 | 55 : 45 | 1·24 | + | + |
| 10 | 70 : 30 | 2·3 | 60 : 40 | 1·5 | ++ | − |
| 14 | 82 : 18 | 4·55 | 68 : 32 | 2·2 | − | − |
| 15 | 76 : 24 | 3·15 | 56 : 44 | 1·27 | + | − |
| 16 | 82 : 18 | 4·55 | 52 : 48 | 1·08 | + | + |
| 21 | 93 : 7 | 13·3 | 48 : 52 | 0·92 | + | − |
| 22 | 85 : 15 | 5·65 | 63 : 37 | 1·71 | + | − |
| 23 | 82 : 18 | 4·55 | 61 : 39 | 1·56 | + | + |
| 24 | 70 : 30 | 2·33 | 72 : 28 | 2·52 | + | − |
| 26 | 82 : 18 | 4·55 | 56 : 44 | 1·27 | + | − |
| 27 | 82 : 18 | 4·55 | 42 : 58 | 0·73 | + | − |
| 28 | 80 : 20 | 4·0 | 56 : 44 | 1·27 | + | − |
| 29 | 84 : 16 | 5·25 | 56 : 44 | 1·27 | − | − |
| 30 | 70 : 30 | 2·33 | 58 : 42 | 1·38 | − | + |
| 32 | 92 : 8 | 11·5 | 63 : 37 | 1·71 | − | − |
| 33 | 92 : 8 | 11·5 | 44 : 56 | 0·77 | ++ | − |
| 34 | 96 : 4 | 24·0 | 74 : 26 | 2·85 | ++ | − |
| 38 | 89 : 11 | 8·1 | 65 : 35 | 1·86 | ++ | − |
| 41 | 93 : 7 | 13·3 | 54 : 46 | 1·17 | ++ | - |

It will be seen that there is a disagreement between the test and the clinical diagnosis in 60·2 per cent. of cases. This group is chiefly composed of those cases which showed no clinical evidence of intestinal ulceration, but gave a positive Triboulet.

We were prepared for some error in the clinical classification, but cannot accept that an error of 60·2 per cent. was present.

The classification of the clinical and post-mortem findings will be made clear from a study of Tables I. and II. One case with definite symptoms of intestinal ulceration and a positive Triboulet showed at autopsy a large tuberculous ulceration in the lower end of the cæcum, with slight involvement of the appendix. The Triboulet was performed on specimens of post-mortem fæces, and whereas that from the small intestine gave a strong positive reaction, the heavily blood-stained specimen from the colon was negative.

It should be observed that the almost complete concord which obtains in the group of 8 cases examined ante-mortem and post-mortem is partly accidental; the total quota of 16 post-mortems show a discrepancy of 37·5 per cent. between Triboulet and post-mortem findings, and by coincidence only 1 of the aberrant cases appears in the last group.

Despite this it is interesting to note that in these 7 cases agreement was complete between clinical diagnosis, post-mortem findings, Triboulet in life and Triboulet post-mortem.

**Conclusion.**

Our clinical finding and biochemical investigation disclose no rational basis for the adoption of the Triboulet test as an aid to the diagnosis of incipient tuberculous ulceration of the intestine.

REFERENCES

1. *Brit. Med. Journ.*, 1934, ii. 100.
2. G. HERTZBERG: *Norsk. Mag. f. Lægevid.*, April, 1934, p. 402.
3. WALLACE AND SALOMON: *Med. Klin.*, 1909, v. 579. (Quoted from Long and Wells, "Chemistry of Tuberculosis," p. 316.)

# CONSULTATION

## CASE

By F. G. CHANDLER,
M.A., M.D. (CANTAB), F.R.C.P. (LOND.),
Physician, with Charge of Out-Patients, St. Bartholomew's Hospital; Physician, City of London Hospital for Diseases of the Heart and Lungs, Victoria Park, E.

On March 23, 1934, I was asked to see in consultation a young lady who was suffering from an acute broncho-pneumonic phthisis of the right upper lobe, which was completely consolidated and already becoming excavated by a cavity of some size. No tubercle bacilli had been found.

The history was as follows: The patient had what was described as a bad cold in December of the previous year, with an infection of the left antrum of Highmore; a troublesome tooth was extracted and all acute symptoms subsided. In January she was not feeling well; twice she had nose-bleeding, but she regained her health. About March 10 she developed a "nasty cough" and was feverish. She went about for three days before consulting her family doctor. When she did so, he found abnormal signs in the right upper lobe and a temperature of 101°. This increased until it reached 103°. No tubercle bacilli were found in the sputum. She was admitted to a nursing home, where the fever persisted and the signs increased. She had night sweats, scanty sputum, a speck of blood on one occasion.

The skiagram showed complete consolidation of the right upper lobe, with a cavity (Fig. 1).

An artificial pneumothorax was advised and induced on March 26. The next day tubercle bacilli were found for the first time. A refill was given on the 29th. The next day the patient looked much worse. She was flushed and cyanosed, the temperature higher. The following day the temperature was 102·4°, pulse 120, respiration rate 40. A pressure was taken and found to be −10−4; no air was given or withdrawn. On March 31 the patient had a profuse hæmoptysis (½ pint in all), with dyspnœa and cough. On April 2, the temperature was 103°, respiration 32, pulse 112.

An X-ray picture taken at this stage showed a further extension of the disease into the right middle lobe (Fig. 2). A refill of 540 c.c. was given, leaving a pressure of $-8-2\frac{1}{2}$. The patient was not distressed after this. On April 5 râles could be heard on the opposite side towards the base posteriorly. A skiagram taken on April 11 revealed an acute spread to the other side

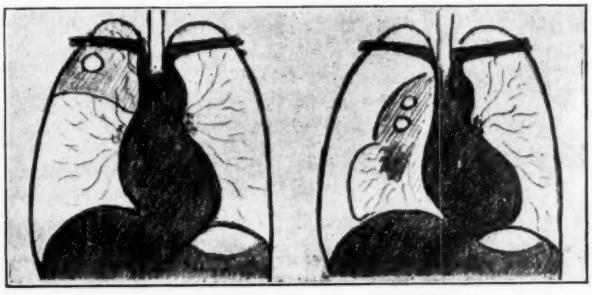

FIG. 1. March 23, 1934.

FIG. 2. April 2, 1934.

(Fig. 3). I was consulted again, and advised gold injections and continuance of the artificial pneumothorax treatment. By this time the faith of the relatives in the treatment, already profoundly shaken, was becoming faint, almost to vanishing point, and we in charge of the case were not a little

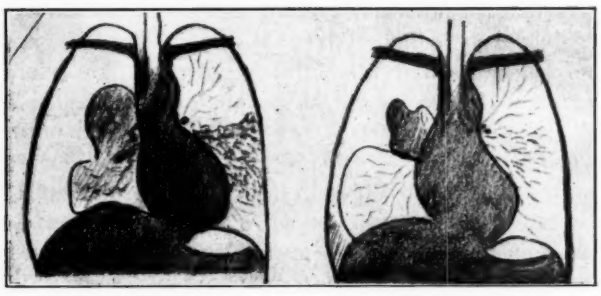

FIG. 3. April 11, 1934.

FIG. 4. May 13, 1934.

anxious. Another opinion was therefore obtained, and this supported strongly the measures adopted, which were considered the only ones that could possibly save the life of the patient.

The pneumothorax was therefore continued, and a solution of gold soluble in water was administered intramuscularly.

By April 13 the patient was better, and the temperature lower, no dyspnœa, colour quite good. By May 7 there was a marked improvement. The temperature was not above 99°, there was no cough or sputum, the patient was sleeping and eating well. The abnormal signs on the left side were disappearing. On May 13 another skiagram was taken (Fig. 4). This showed an excellent selective collapse of the right lung, and a very decided clearing of the abnormal shadows on the left side. In June she went to a sanatorium and made a steady and progressive improvement. By September she was able to be up for a short time daily; by December she was continuing to make good progress and able to take a " considerable amount of exercise."

A little fluid developed on the pneumothorax side. A later report (April of the following year) stated that the patient's general condition had steadily improved; the fluid had entirely absorbed; she was walking one and a half miles each day; and she was looking exceedingly well and feeling better than she had done for years.

## CLINICAL CASES

# AN UNUSUAL CASE OF TUBERCULAR SPONTANEOUS PNEUMOTHORAX

REPORTED BY GERALD RAMAGE,
M.D., D.P.H.,
Assistant M.O., Baguley Sanatorium, Manchester.

THE main interest in the case described below is the right spontaneous pneumothorax, now carried on as an artificial pneumothorax for four and a half years. She was admitted to Withington Hospital suffering from a right spontaneous pneumothorax and was soon transferred to Baguley Sanatorium, where the pneumothorax was converted. Later it was abandoned and the patient took her own discharge. On entering Rufford Hospital, the pneumothorax was re-established and, owing to contralateral disease, the left lung was collapsed. She was transferred to Baguley Sanatorium, where she is now.

Mrs. A. H., aged 21 years, became ill in 1930. Patient dates the start of her illness from her confinement. In early 1930 she noticed an unusual tiredness and occasional loss of appetite. Cough and loss of weight appeared later.

In May, 1930, her throat started to feel dry and once on coughing she brought up a small clot of blood mixed with sputum. This was followed by loss of voice for about seven days. Towards the end of the month, while wheeling a perambulator, she was seized with an acute right-sided pain and sudden dyspnœa. Her doctor diagnosed pulmonary tuberculosis and tubercle bacilli were found in the sputum.

She was admitted to Withington Hospital on June 10, 1930. She had a considerable amount of purulent sputum; there was some dyspnœa on exertion and occasional night sweats. Her voice was hoarse.

*Clinical Findings.*—Displacement of the heart about 2 inches to the left. Breath sounds were inaudible over the lower right chest and diminished movement was observed. The left lung showed prolonged expiration only. Right spontaneous pneumothorax was diagnosed. Her temperature chart

remained level at 97° and pulse rate 100 to 120 per minute. She was graded T.B. +1, and on August 14, 1930, was transferred to Baguley Sanatorium. Then the temperature showed an evening rise of 100°. Two ounces of sputum was expectorated each day and tubercle bacilli again found. Her weight was 6 stone. She received treatment for her larynx, which showed chronic inflammation of the arytenoids. By September 15, 1930, the temperature had settled and the sputum lessened to ½ ounce. Examination of the chest showed that the air was absorbing and the heart returned ½ inch towards its normal position.

On October 8, 1930, screening revealed a tuberculous infiltration of the right apex and air and fluid in the pleural space. This fluid increased in amount, and on October 26 200 c.c. were removed and air replaced. Readings: −3 ±0, 350 c.c. air, ±0 +3. A few days later 750 c.c. muddy fluid were aspirated and air replacement performed. A further two refills were done without any fluid being found on exploration, but on November 26 10 c.c. of yellowish flaky fluid were aspirated and gas replacement performed. From October to this date there was pyrexia up to 100° and 101° at night, though these did not follow the gas replacements. Her condition was fair and crepitations became audible on the left side. It was concluded that disease was active on that side also, and so the refills were discontinued.

The patient's condition started to improve. Her temperature remained steady, sputum was reduced to ½ ounce, and her weight began to increase slowly. Frequent sputum tests had proved positive, but in April, 1931, three successively negative sputum tests were obtained, although bacilli were profuse in the effusion, which was then purulent. By May the patient had recovered sufficiently to be allowed two days' leave from the sanatorium. She was afebrile, but had a pulse rate of about 100. Her weight had increased from 6 stone to 7 stone. In June 550 c.c. pus were aspirated, and this left a small sinus which healed up by the following August. Two further aspirations were done in July.

In January, 1932, she took her own discharge against advice, and came under the Lancashire County Council. She continued her housework and remained well until March, 1932, when she suffered pleurisy pains in the left side of her chest, and, still having fluid in the right chest, she was recommended to undergo further treatment. She was admitted to Rufford Pulmonary Hospital on March 24, 1932. Her sputum was positive and the right pleural cavity was almost full of a purulent effusion; 2,250 c.c. of pus were aspirated and 950 c.c. of air replaced, and the aspirations were repeated at lengthening intervals and the fluid became thinner. Refills were given monthly and about 200 c.c. of air introduced.

Skiagram 1 shows the condition of the chest in September, 1932. The fluid on the right side shows the accumulation for three months. Infiltration and cavitation is visible at the apex of the left lung.

Induction on the left side was performed on September 26, 1932, and skiagram 2, taken on January 16, 1933, shows a good collapse on this side. This was maintained by refills of about 500 c.c. fortnightly. A left effusion developed, and in May 430 c.c. of clear fluid were aspirated and a further 900 c.c. in June. The patient was again transferred to Baguley Sanatorium. Before discharge from Rufford Hospital she was afebrile and had a pulse rate of 76 to 96 and was able to walk half a mile. Two consecutive positive sputum tests were obtained and she complained of slight dyspnœa on walking.

Skiagram 3, taken in October, 1933, shows the bilateral pneumothorax and a small amount of fluid. Small calcified nodules are visible in the right apex. The cavity in the left apex is completely obliterated. Blood sedimentation showed a drop to 18 mm. in one hour in November, 1933.

January 18, 1934: Gas replacement left side; 480 c.c. of clear greenish fluid removed. A few days later the patient was restricted to bed on account of loss of weight (from 6 stone ½ pound to 5 stone 11 pounds). She was still afebrile, but the pulse rate had increased to 90-98.

February, 1934: Blood sedimentation rate shows an improvement of 2 mm. in the hour. Activity of patient was gradually increased until in June she was up eight hours per day and doing two hours' light handicraft.

July, 1934: Sedimentation rate remained at 18 mm. in one hour.

Skiagram 4 shows the condition in January, 1935. The patient is afebrile and has an average resting pulse rate of 90 per minute. Her weight is 6 stone. She has 2 ounces of sputum, and this was positive on January 15, 1935. Blood sedimentation rate is 19·5 mm. in one hour. There is a small quantity of clear fluid on both sides, which has been stationary for months. Small refills are given at monthly intervals on the left side and the right side is being allowed to re-expand. The last readings are:

| | | | | | | |
|---|---|---|---|---|---|---|
| Left (January 29, 1935) ... | ... | −15 | −3 | 150 c.c. | −10 | ±0 |
| Right (December 20, 1934) | ... | −20 | −2 | 100 c.c. | −6 | +2 |

She is up twelve hours (inclusive of one hour and forty minutes' rest) and does one hour light ward work and two hours' handicraft per diem.

Her appetite is fairly good, and she is able to take part in all the hospital activities, and, despite some dyspnœa on exertion, appears to enjoy life.

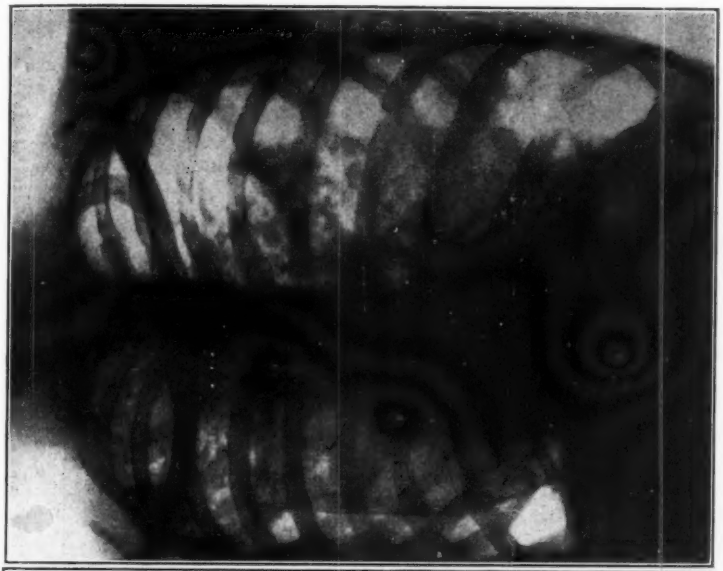

FIG. 2.

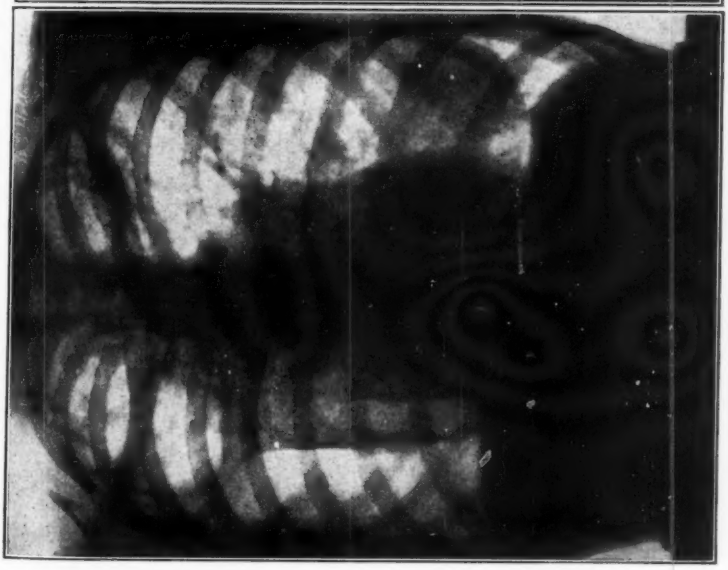

FIG. 1.

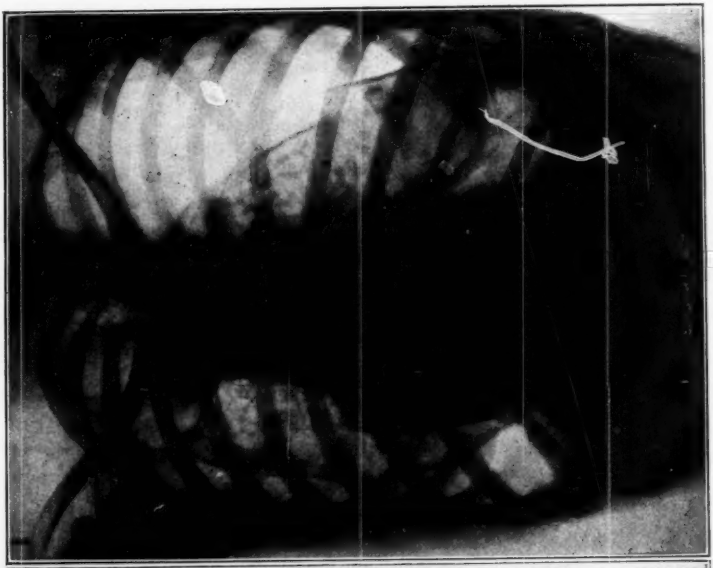

FIG. 4.

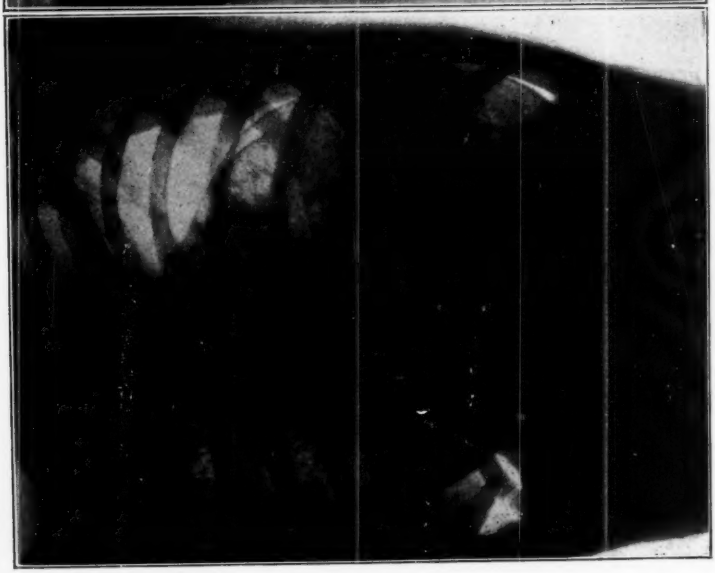

FIG. 3.

**Literature.**

The general opinion of the prognosis of spontaneous pneumothorax complicating pulmonary tuberculosis is expressed by West[10] in his summary: "75 per cent. die within the first fourteen days, about 90 per cent. before the end of the month, though the duration of the life of the remaining 10 per cent. may be considerable." Fishberg[2] agrees with this, while Wingfield,[12] Happel,[3] and Symes Thompson[9] state that the prognosis is bad. The largest series of cases investigated that was obtainable was that of J. A. Wilson,[11] while numerous workers report single or a few cases only a few months after their onset.

Wilson investigated 107 cases and classified them:

Class I.: Complete collapse with mediastinal displacement.
Class II.: Complete collapse without mediastinal displacement.
Class III.: Incomplete collapse with mediastinal displacement.
Class IV.: Incomplete collapse without mediastinal displacement.
Class V.: Undetermined.

| *Class.* | *No.* | *Dead.* | *Alive.* | *Average Life.* |
|---|---|---|---|---|
| I. | 42 | 30 | 5 | 3 years 4 months. |
| II. | 4 | 2 | — | — |
| III. | 27 | 20 | 5 | 2 years 1 month. |
| IV. | 16 | 8 | 5 | 1 year 8 months. |
| V. | 8 | 6 | 1 | 9 months. |

Leggett, Myers, and Levine[6] reported ten cases, in six of whom the spontaneous pneumothorax was a terminal condition and all died, with the exception of one mentioned below. One of the others was lost sight of. One in whom the spontaneous pneumothorax was the first symptom of pulmonary tuberculosis is alive and working after four years. The third spontaneous pneumothorax was considered idiopathic at first and pulmonary tuberculosis was not diagnosed until five years after the spontaneous pneumothorax. The last case was an advanced case of tuberculosis and is mentioned below.

Hazen[4] reports a case which was observed for three years and eight months and was discharged "in the same physical condition as before the spontaneous pneumothorax occurred."

Kalin[5] and Stewart[8] each report a case in which the patient's condition was improved by the occurrence of spontaneous pneumothorax.

None of the above cases were continued as artificial pneumothorax cases. Referring to such cases, Fishberg remarks that they "do not terminate so favourably as one induced for therapeutic purposes." Most of the cases traced in the literature developed fluid in the pleural space.

The case of advanced pulmonary tuberculosis mentioned above was first seen two years after his spontaneous pneumothorax. Fluid was present

and gas replacements continued. He was alive when reported—three and a half years after the onset.

Macfie and Osmaston[7] treated an open case of tubercle who had a spontaneous pneumothorax with gas replacements for three months. Happel also reported a case being continued for three months. Aspen[1] and Symes Thompson each report a case treated with gas replacements and alive in three years and three months, and two years respectively. In both cases the fluid contained tubercle bacilli. Aspen's patient was washed out with gentian violet.

In the literature available no case of spontaneous pneumothorax was found who was alive and well four years after the onset. Further, no such case was encountered with the bilateral collapse. These features make this case one of exceptional interest.

My best thanks are due to Dr. H. G. Trayer, Medical Superintendent of Baguley Sanatorium, near Altrincham, for suggesting and permitting the above report; and to Dr. C. W. Laird for permission to use his X-ray photographs and data.

## REFERENCES

1. Aspen, G. P.: Tuberculous Empyema secondary to Spontaneous Pneumothorax, with Apparent Recovery, *U.S. bet. Beir. M. Bull.*, July, 1929, v. 538-540.
2. Fishberg, M.: Pulmonary Tuberculosis, 4th ed., 1932.
3. Happel, J. H.: Spontaneous Pneumothorax in Tuberculosis, *U.S. bet. Beir. M. Bull.*, November, 1926, ii. 1032-1036.
4. Hazen, C. M.: Bilateral Spontaneous Pneumothorax with Tuberculosis and Recovery, *U.S. bet. Beir. M. Bull.*, July, 1928, iv. 628-630.
5. Kalin, M.: Spontaneous Pneumothorax in Tuberculosis, *N.Y.M.*, October 12, 1918, cviii. 632 (quoted by Leggett, etc.).
6. Leggett, E. A., Myers, J. H., and Levine, J.: Report of Thirty-one Cases of Spontaneous Pneumothorax, *Amer. Rev. Tub.*, March, 1934, xxix. 348-361.
7. Macfie, J. D., and Osmaston, R. L.: Case of Spontaneous Pneumothorax treated with Gas Replacements, *Lancet*, November, 1927, ii. 967-968.
8. Stewart, H. R.: Spontaneous Pneumothorax with Unusual Features, *Med. Bull bet. Admin.*, 1932, p. 220 (quoted by Leggett, etc.).
9. Symes Thompson, S. A. E.: Spontaneous Pneumothorax Case, *Lancet*, October, 1930, ii. 791-793.
10. West, S.: A Contribution to the Pathology of Pneumothorax, May 3, 1884 (quoted by Leggett, etc.).
11. Wilson, J. H.: Brief Statistical Summary and Discussion of Cases of Spontaneous Pneumothorax in Fitzsimmons General Hospital, Denver, *Amer. Rev. Tub.*, November, 1926, xiv. 567-585.
12. Wingfield, R. C.: Textbook of Pulmonary Tuberculosis, 1929.

# AN EPITUBERCULOUS LESION IN ASSOCIATION WITH SCARLET FEVER, SHOWING CHANGES IN THE BLOOD SEDIMENTATION RATE

By J. H. F. PANKHURST,
M.D., B.HY., D.P.H. (DURH.),
Assistant Medical Officer of Health, Stockport.

*Case History.*—P. H. (female), æt. 10 years, was admitted to hospital with scarlet fever on the third day of disease. The illness was of a mild type clinically, and the rash and tonsillitis subsided within forty-eight hours of the administration of 10 c.c. scarlet fever antitoxin. Progress was thereafter normal until the tenth day, when the temperature began to rise. The cause of this remained obscure until the fourteenth day, when localised bronchial breathing was found at the right side of the sternum, occupying a small circular area centred over the third costochondral joint. There was diminished resonance over this lung field, but no adventitious sounds, no dyspnœa, and only slight cough without sputum. The bronchial breathing was clearly audible for twelve days, and then gradually decreased in intensity. The temperature reached normal limits by the twentieth day. An X-ray was taken during the period when bronchial breathing was at a maximum and showed the characteristic appearances of an epituberculous lesion—namely, a wedge-shaped homogeneous opacity spreading out into the right upper lobe from the lung root. It was not possible to obtain sputum for examination, and search of the fæces for tubercle bacilli proved negative. The intradermal tuberculin test was strongly positive on the twentieth day.

This case was one of a number of scarlet fever patients under observation for changes in the blood sedimentation rate (Westergren's method). The actual amount of sedimentation after one hour (sedimentation index) is not constant in scarlet fever, and varies with the individual patient and the stage of the disease. But if daily values of the sedimentation index are plotted in graph form the nature of the curve produced is fairly typical for uncomplicated cases. An example of a normal curve was contrasted with the sedimentation rate changes of the patient under review, and it was seen that, compared with the relatively low values recorded for the few days after admission, the index rose rapidly with the onset of the pulmonary lesion

and had not returned to normal (under 10 mm.) even after forty days. At this stage there were no abnormal signs and the girl appeared well.

The pathology of the case remains obscure in the absence of definite knowledge of the nature of an epituberculous lesion. It is possible that atelectasis secondary to bronchial obstruction produced by pressure of an enlarged mediastinal gland was the cause, but it is equally possible that the process was an acute benign pulmonary tuberculosis following the sudden lowering of a normally high immunity by the onset of scarlet fever.

I wish to express my thanks to Dr. J. C. H. Mackenzie, Medical Superintendent of the Isolation Hospital and Sanatorium, Leicester, where I had the opportunity of studying this case.

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# SPONTANEOUS PNEUMOTHORAX FOLLOWING THERAPEUTIC PNEUMOTHORAX

REPORT OF CASE BY H. G. TRAYER,
Medical Superintendent, Baguley Sanatorium,
AND C. H. WADE,
Medical Officer, Baguley Sanatorium.

THE patient, a man 28 years of age, was admitted to Baguley Sanatorium with cough and blood-stained sputum containing tubercle bacilli. His temperature was normal and his pulse rate 82 per minute. His weight was 2½ stone below his normal average of 12 stone.

There were signs of a cavity at the right apex and moist sounds over the whole of the left lung.

The skiagram confirmed the presence of a right apical cavity. There was patchy mottling below this, suggesting cavitation, and the root shadow was extensive. The left lung root and bronchial shadows were also well marked and the left upper lobe infiltrated, a ringed appearance due to fibrosis being clearly visible. Screening showed a diminished diaphragmatic excursion on both sides. Ten days after admission he coughed up 1½ ounces of blood and larger amounts during the next week, culminating in a total of 12 ounces during one night. Because of the acute distress and anxiety

shown by the patient, a right pneumothorax was then induced, although there was some doubt as to which lung was bleeding.

Three hours later an obvious right spontaneous pneumothorax occurred after a spasm of coughing. It did not become acute until early the next day, following defæcation, an act which preceded many of his attacks of hæmoptysis, although straining had been avoided by keeping the bowels gently relaxed with aperients. A pneumothorax needle relieved the immediate symptoms and the pressures were left at − 1 +1 (an early reading was +8 +20). The condition recurred within half an hour and it was necessary to fix up permanent drainage with an under-water seal.

On the fifth day the lung could be felt against the needle, the position of which had been changed at intervals. It was, therefore, removed and firm strapping applied. A skiagram showed a more extensive lesion than previously, but no evidence of pneumothorax or effusion. The re-expansion of the lung was followed by further hæmoptysis, and the patient's general condition became extremely poor. During the week following induction, however, there had been neither sputum nor hæmorrhage, and the temperature was normal.

The next few days were, however, marked by hæmoptysis of increasing amount, and a second induction was performed on the right side.

Firm strapping was applied after introducing 100 c.c. of air. The manometer readings were − 15 − 5 initially and − 13 − 1 finally. The patient coughed up 6 ounces of blood the next day, and he had a feeling of tightness and discomfort on the right side of the chest. The pressures were now − 6 +6, which implied a leakage of air into the pleural space. A refill was not given, and subsequently the pressures remained the same and the condition did not demand any interference.

The temperature, however, rose for the first time in two weeks following the first induction, reaching 98·8° in the evening and 102° the next day. Aspiration broncho-pneumonia was diagnosed and the patient died a week later.

**Necropsy.**

*Right Pleural Space.*—There were many recent pleural adhesions and two firm bands—one anterior near the second interspace, one posterior running out to the axilla—and a terminal effusion of about 2 ounces of clear fluid.

*Right Lung.*—There was a small orifice on the anterior aspect of the middle lobe, surrounded by fibrinous exudate. It lay in a furrow caused by adjacent fibrosis and could easily have become valvular. There did not appear to be an active focus of disease in the lung at this point. Cavitation involved the top half of the upper lobe and also the apices of the middle and lower lobes.

There was little secretion present. Chronic fibroid disease with scattered caseating tubercles was present elsewhere.

*Left Pleural Space.*—Adhesions were present at the apex and vertebral border, and there were also a few basal attachments.

*Left Lung.*—In the upper lobe was a subapical cavity, the size of a hazel nut, filled and closed by a partly organised blood clot which covered the ragged edges of an opening in the wall of an artery. This was without any doubt the source of the hæmorrhage. In the apex of the lower lobe was a cavity partly filled with blood aspirated from the one above. Acute broncho-pneumonia involved the remainder. The hilar glands were much enlarged and showed softening.

Lesions were not found elsewhere.

**Commentary.**

The necropsy showed clearly that the hæmorrhage came from the left side and yet a right-sided pneumothorax was completely successful in the first instance in checking the hæmoptysis. The small cavity in the left subapical region, the source of the hæmorrhage, was situated on the medial aspect of the lung, and did not appear to bear any relation to the large annular shadow visible in the first skiagram. It was not possible to control the lung after the spontaneous collapse had occurred, because the air leak remained valvular until the visceral pleura was again in contact with the parietal layer and the lung was then fully expanded.

It is remarkable that after so much interference and with so extensive a lesion an effusion did not develop, and that the condition was apyrexial until a late stage was reached.

Spontaneous pneumothorax is an unfortunate complication exhibited in a small but definite proportion of cases undergoing treatment by artificial pneumothorax. The Matsons[1] recorded sixteen cases in a series of 480, a rate of 3 per cent., and Morgan[2] points out that more systematic screening after induction or attempted induction would reveal an even larger percentage. The records of this sanatorium show that there were four such cases in a series of 183, and all four ended fatally.

*The cause* has been stated to be laceration of the visceral pleura by the needle or rupture of an emphysematous bulla,[3] but in the present case the site of induction was well removed from that of the air leak, and the post-mortem appearances suggest that tearing of an adhesion was the most likely reason. This happened in spite of the small amount of air (100 c.c.) introduced, and the general principles of low tension pneumothorax carried out. It is noteworthy that the middle lobe is considered to be the least frequently

involved in adhesions. The records show that adhesions were present in all four cases mentioned above, and post-mortem examination confirmed the fact that a tear was present in two. A necropsy was not done in the remaining two cases.

Liability to a tear would appear to be greatest at the commencement of artificial pneumothorax, but two of the four cases had been under treatment for six months before the spontaneous pneumothorax occurred. Tearing of an adhesion in partial pneumothorax cases is a relatively common occurrence, as evidenced by a varying degree of discomfort for the patient at the time, and often results in perforation of the lung and effusion, simple or purulent. Two such instances were furnished recently by pneumothorax cases. Adhesions known to be present from screening records disappeared, allowing more complete collapse of the lung and resulting in a simple effusion in one case. Spontaneous pneumothorax, however, does occur from the same cause, as shown by the case here described, and by details of similar cases in the records of this sanatorium.

## REFERENCES

1. R. W. Matson, R. C. Matson, and M. Bisaillon: *Journ. Amer. Med. Assoc.*, 1923, lxxxi. 713.
2. W. P. Morgan (quoted by Fishberg): Pulmonary Tuberculosis, p. 508.
3. F. Parkes Weber: Mitchell Lecture, *Lancet*, November 5, 1921, p. 940.

# MEETINGS OF SOCIETIES

## THE TUBERCULOSIS ASSOCIATION

THE provincial meeting of the Tuberculosis Association was held at Oxford on April 11, 12, and 13. The President, Dr. L. S. T. Burrell, was in the Chair, and 132 members were present.

The first session was opened by Dr. Gravesen, who read a paper on " The Surgical Treatment of Pulmonary Tuberculosis." He suggested that the important factor in collapse therapy was relaxation and not compression of the lung. The ideal in pneumothorax treatment was to collapse the diseased portion of the lung, and this is known as selective collapse. It often happens that owing to adhesions the diseased part does not collapse, but the healthy part does, and this Dr. Gravesen described as contra-selective collapse. In bilateral disease it is often possible to produce relaxation of the lung or partial collapse by a combination of methods. Thus apical thoracoplasty, for which he suggested the term cupuloplasty, might be helped by freeing the apex without plugging as in apicolysis. This would cause vertical as well as horizontal relaxation. He regarded phrenic evulsion as of very limited value and did not consider it indicated in the treatment of apical cavities.

Mr. J. E. H. Roberts thought that relaxation was not the only factor; lymph-stasis was important, and some degree of compression was also needed if cavities were to be collapsed. He agreed that a contra-selective collapse was often continued far too long in this country, and that if the diseased part of the lung would not collapse by pneumothorax it was usually best to abandon the treatment and adopt some surgical means of collapse.

He thought the cauterisation of adhesions ought to be practised more often and preferred the electro-cautery to diathermy, except to stop bleeding, as it was not so likely to lead to the formation of effusion. He regarded it as dangerous to cut adhesions if tubercles could be seen on them.

Mr. Tudor Edwards thought that phrenic evulsion, or at least crushing, was worthy of more popularity. It will heal a proportion of small apical cavities, and in combination with artificial pneumothorax may save the

necessity of thoracoplasty. He regarded it as a wise procedure before a total but wrong before a partial thoracoplasty.

Dr. Morriston Davies agreed that a contra-selective collapse was useless. He said that prolonged bed rest might avoid surgical treatment or artificial pneumothorax and might in the end even save time. He thought that phrenic evulsion had its place in treatment, but was of no use if there was a thick interlobar septum.

Professor Jacobæus then read a paper on "Bronchospirometry." He showed an instrument by means of which air could be taken separately from either lung. By this means the function of each lung can be determined, and this is of special value in cases of artificial pneumothorax or thoracoplasty.

In the evening the President's reception was followed by the Annual Dinner in the hall of Exeter College.

On Friday, April 12, Dr. R. R. Trail gave an address on "Tuberculous Effusions and Empyemata." For a simple effusion he advocated rest until absorption, and then sanatorium treatment. At Midhurst between 1926 and 1933 only two out of sixty-one cases treated in this way developed further signs of tuberculosis.

When an effusion complicated artificial pneumothorax, he thought continuous replacements should be avoided if the fluid remained clear. Gradual obliteration of the pneumothorax cavity might take place, but it started at the bottom or healthy part, the upper zone was the last to be drawn out, and end results were quite good.

Dr. Gravesen said that clear effusion complicating artificial pneumothorax did no harm. The so-called idiopathic pleural effusion was tuberculous, and he thought the percentage of later pulmonary tuberculosis would be much reduced if in all cases the fluid was aspirated, replaced by air, and a pneumothorax maintained.

Dr. Maurice Davidson pointed out that in cases of pleural effusion the pulmonary focus was often at the apex of the opposite lung, and he did not advocate converting a pleural effusion into an artificial pneumothorax as a routine method of treatment.

Professor Lyle Cummins suggested that an effusion followed an allergic inflammation in the pleura; in cases of pneumokoniosis there might be extensive pleurisy, but effusion was very rare.

A discussion on "Dyspnœa" and its significance in the treatment of pulmonary tuberculosis was then held, and Dr. Boland read an interesting paper by Dr. E. P. Poulton, who, unfortunately, was prevented from attending. Dr. R. Hilton said how extremely complex the problem of dyspnœa was, and even in complete pneumothorax there is still some movement of

the lung unless it is entirely fixed by thickened pleura. Dr. W. Stobie then read a paper dealing with the varieties of dyspnœa and their treatment, and a full discussion followed.

On the Saturday morning Dr. R. A. Young opened a discussion of a clinical case. Dr. Geoffrey Marshall followed, and an interesting discussion in which many members participated took place.

Cinematograph films of Burrow Hill Sanatorium Colony and of the Welsh National Memorial were next shown, and the session concluded with the Annual Meeting.

A meeting was held at Manson House on Friday, May 17.

Mr. H. P. Nelson opened a discussion on the value of phrenic operations. He said that this operation has a definite place in the treatment of pulmonary tuberculosis, but should never take precedence to artificial pneumothorax. The effect of phrenic paralysis is to raise the diaphragm and so relax the lung. This is of special value in cases where artificial pneumothorax has been induced and the lung is stretched between apical and basal adhesions. He thought that the immediate improvement which so often followed the operation was not maintained in many cases. It was valueless for thick-walled cavities, but 63 per cent. of thin-walled cavities of less than 1 inch diameter closed after phrenic evulsion.

The contraction of the abdominal muscles during cough gives a strong push to the paralysed diaphragm, and so assists expectoration, but after a time, as the diaphragm becomes fibrotic, this effect is lost.

Dr. Peter Edwards said that the greater the rise of the diaphragm the better the results. He prefers artificial pneumothorax to phrenic paralysis, but regards the latter as of considerable value, and has never seen it do harm. It is the best method of relieving pain or cough from diaphragmatic adhesions. By relief of tension it may check recurrent hæmoptysis. He regarded it of great value in the treatment of apical cavities, especially if combined with artificial pneumothorax. Other indications for phrenic paralysis during pneumothorax treatment are to lengthen the intervals between refills, to relax the lung in cases of adhesions, to control fluid, to correct mediastinal hernia or flop, and at the termination of the treatment to raise the diaphragm and prevent too much compensatory emphysema.

A discussion followed in which many members took part.

Dr. Peter Kerley opened the evening session with a paper on the technique of radiography of the chest. Whilst admitting the value of the recumbent position, he pointed out the advantage of the erect position in X-ray examination of chest cases. He stressed the importance of a quick exposure, and showed many interesting and excellent skiagrams.

Dr. J. V. Sparks thought that the prone position was usually better than the erect for these cases. He agreed as to the necessity of speed in taking the films, and showed a series of first-class skiagrams taken in a small fraction of a second.

The discussion which followed largely reverted to the old problem of annular shadows and their origin. Undoubtedly most of these are cavities, but some appear to be emphysematous bullæ, and may resemble cavities very closely even to the extent of having a fluid level.

# REVIEWS OF NEW BOOKS

*Nutrition and Disease.* By EDWARD MELLANBY, M.D., F.R.C.P., F.R.C.S., Secretary of Medical Research Council. Pp. 171 and 61 illustrations. 1934. Price 8s. 6d. Edinburgh: Oliver and Boyd.

This book represents the substance of the Cromian Lectures to the Royal College of Physicians, and also of the Linacre Lecture at Cambridge delivered in 1933.

The author has had the advantage of being both physician and professor of pharmacology at a large general hospital, so that his laboratory investigations are combined with their clinical applications.

The first two chapters deal with rickets and dental structure. It is suggested that a tendency to pyorrhœa may be produced by deficiency of vitamin A, and that cereals play a part by inducing a defective formation of gingival epithelium.

In Chapter III. a full account of simple and toxic goitres is given. Their prevention and treatment and the effect of iodine on the thyroid under various conditions are discussed at length.

Chapter IV. deals with nutrition and infection. The author shows that vitamin A is particularly concerned with the defence of epithelial surfaces, including those of the respiratory tract. It was found that children with measles who were treated with vitamins A and D had a lower mortality from pulmonary but not from otological complications.

Tuberculous infection appears to be influenced by fat-soluble vitamins, and septic lesions are liable to develop if there is a deficiency of vitamin A or carotene.

The two concluding chapters are devoted to the relationship between nutrition and degenerations in the nervous system.

The book is full of interest, and contains many illustrations which are beautifully reproduced.

*Etude clinico-bacteriologique sur la possibilité de déceler la présence de bacillus tuberculeux chez l'enfant par la méthode du lavage de l'estomac.* By NILS LEVIN. Pp. 108. 1934. Stockholm: Isaac Marcus Boktryckeri-Actiebolag.

The fact that children almost always swallow any sputum they may have makes bacteriological proof of the presence of tuberculosis more difficult than in the adult. The author of the above thesis concludes, as the result of his investigations, that gastric lavage, followed by culture or better by guinea-pig inoculation, is greatly superior to the more usual examination of the fæces.

In all 457 children were examined: of these 40 controls negative to tuberculin all gave negative results on lavage. Of the remaining 417 children positive to tuberculin, 249 were found positive on lavage. In positive cases direct examination of the lavage fluid rarely showed the presence of tubercle bacilli; culture gave 32·7 per cent. positive and guinea-pig inoculation 94·6 per cent.

The clinical material was carefully controlled by X-ray examination, a large number of films being clearly reproduced. This study showed that out of 108 children whose tuberculosis was apparently inactive, only one gave a positive result on lavage, whereas in active cases bacilli were found in 155 out of 226 cases (69 per cent.).

The cases were then grouped according to the type of lesion present. In 16 cases the glands at the root of the lung appeared to be the only lesion present; 4 of these cases were positive (25 per cent.). In 74 cases the glandular enlargement was accompanied by infiltration of the prehilar region; in 41 of these cases tubercle bacilli were present (55 per cent.). The cases in which the lesions were in the lung parenchyma were divided into primary, secondary and tertiary stages (Ranke). In the primary and secondary stages there were 78 positive cases out of 103 (76 per cent.). In 33 children with tertiary stage lesions 32 were positive (97 per cent.).

*Thérapeutique hydro-climatologique de la tuberculose.* By Léon Bernard and R. Even. Pp. 146. 1934. 20 fr. Paris: Masson.

The above booklet forms one of a series by different experts dealing with spa and climatic treatment of various diseases. As might be expected, the first section of the book is brief, as the authors hold that in the treatment of all active forms of pulmonary tuberculosis balneology has no place.

The greater part of the book is taken up with a description of the climate of France, with special reference to the suitability of the various regions for the treatment of tuberculosis. Humidity of the ground is considered more favourable than dampness of the air, and the stimulating influence of high altitudes is looked on as being suitable for the torpid case and contra-indicated in the acute.

The well-known prejudice of French writers against the seaside resort in the treatment of phthisis appears to be well founded, so far as France is concerned, as the northern and western coastal regions are on the whole humid and exposed to rain-bearing winds. The Riviera resorts, once so popular on account of their sheltered situation and high sunshine record, are subject to sudden variations of temperature, and provide such unsuitable distractions that they cannot be recommended for the majority of patients. For those unsuitable for treatment in the High Alps, suitable climate may be found at a moderate altitude in the hinterland of the Riviera or in the lower valleys of the Pyrenees.

This book will, unfortunately, be the last contribution to medical literature of its senior author, the late Professor Léon Bernard; it may be confidently recommended as a guide to the climatic treatment of tuberculosis in France.

*Allergy and Applied Immunology*. By WARREN T. VAUGHAN, M.D. Second Edition. Pp. 420. 1934. Price 21s. London: Henry Kimpton.

The problem of allergy is one of considerable importance not only as regards the so-called allergic disease such as asthma, but in most microbic diseases such as typhoid fever and tuberculosis, where infection produces general changes in the cells of the body.

Dr. Victor C. Vaughan's explanation of anaphylaxis and allergy does not explain all the facts as known today, but may be taken as a good working hypothesis. He suggests that when a living cell comes into contact with a foreign protein it will produce an enzyme or ferment to digest the foreign protein, splitting it up into its constituent amino-acids and using those required for its own nutrition. This takes place slowly, but having acquired the power to produce an enzyme for the particular foreign protein when it once more comes into contact, the protein is rapidly broken up and a quantity of poisonous bodies are liberated.

The first part of the book is a general discussion on allergy. Part II. is a detailed description of many allergens and antigens, animal, vegetable, various dusts and drugs, and the part played by geographical location. Much space is given to the various food groups.

This is followed by a full account of diagnosis and prognosis and treatment, with final chapters dealing with the manifestations of allergy and methods of producing immunity.

The book, which is intended for the patient as well as the doctor, is full of interest, and is well produced and illustrated. It concludes with a good bibliography and index.